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MANUAL

OF

PATHOLOGY

INCLUDING BACTERIOLOGY, THE TECHNIC OF POSTMORTEMS, AND METHODS OF PATHOLOGIC RESEARCH

BY

W. M. LATE COPLIN, M.D.

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BEING A SECOND EDITION OF THE AUTHOR'S "LECTURES ON PATHOLOGY," REWRITTEN AND ENLARGED

With Two Hundred and Sixty-eight Illustrations

MANY OF WHICH ARE ORIGINAL

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PREFACE TO SECOND EDITION.

During the winter of 1894 and 1895, Messrs. P. Blakiston, Son & Co. published, in serial form, abstracts of the writer's lectures entitled "Lectures on Pathology." At the close of the college session, the fasciculi were bound and the resulting volume placed on the market. Very much to the surprise of the publishers, as well as of the writer, the edition lasted less than nine months. It was exhausted at a time when the teaching of the college year precluded the revision which the matter so much needed. During the past six months the entire book has been revised, the larger part having been entirely re-written. The first edition contained 250 pages and 51 illustrations; the present volume, in the face of every effort to condense without sacrificing accuracy, has reached 638 pages and contains 268 illustrations. The most difficult problem has been to keep the volume from assuming undesired dimensions, and, now that the work is completed, the writer wishes to say, parenthetically, that a volume of twice the size could have been produced with probably less labor. Being practically a new book, there are, no doubt, typographic and grammatic errors. The writer acknowledges in advance his appreciation of any communication calling his attention to such lapses.

In the publication of the original fasciculi, the writer was favored by the aid of Prof. Kyle and Dr. Bevan. Prof. Kyle wrote the fasciculus on "Tumors" and Dr. Bevan the article on "Bacteriology." In the revision of the work, both articles have been somewhat enlarged, but the thoroughness of the original

has not demanded any extensive revision. There have been made some additions and a re-arrangement of subjects, in order to secure greater conformity with the remainder of the book. In the original, acknowledgment of the assistance was given with the fasciculi; it is now incorporated here.

Practically, all the added illustrations appear for the first time in a work on pathology in the English language. The source is credited with each cut. Of the original illustrations, it is not the author's province to speak. They have been prepared in the writer's laboratory from specimens and slides of which the clinical and pathologic histology were fully known. In this connection the writer wishes to acknowledge the invaluable assistance of Prof. H. F. Harris, who personally superintended the execution of most of the original drawings. Miss E. G. Harding, artist, has, with great patience, made the original drawings, often re-drawing an illustration a number of times before submitting it for approval.

To Drs. R. C. Rosenberger and W. P. Read the author wishes to acknowledge valuable aid in proof-reading and other detail work in the completion of the volume.

Instead of the usual method of inserting a table of illustrations, arranging the figures in the same order as they appear in the pages, an alphabetic list, by subjects, is inserted, for the arrangement of which I am indebted to Mr. L. H. Prince.

In conclusion, the writer wishes to submit the volume, not as a treatise or book of reference, but, as its title indicates, as a manual which he hopes may be useful in the laboratory, postmortem room, and in clinical diagnosis by the aid of the microscope. To attain, as fully as possible, the last-named aim, the chapters on the microscopic examination of tissues, blood, and urine have been most fully illustrated.

Thanking the profession for its kindly reception of the previous edition, this volume is respectfully submitted for consideration.

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INTRODUCTION.

Pathology bears the same relation to our study of disease that physiology does to our knowledge of those complicated phenomena which we call life. Physiology deals with the normal processes,—the functions of organs and tissues in health,—while pathology is a study of those phenomena which we designate as disease. Physiology is the science of normal life; pathology is the science of abnormal life—disease. It has been said, and quite truly, that pathology is morbid physiology—the physiology of disease. The two subjects demand associated study, as from a knowledge of one we acquire much information bearing either directly or indirectly upon the other. The more we study the intricate problems of morbid processes, the relations of tissue change to alteration of function, and the fuller our knowledge of the normal, the more apparent the association of pathology and physiology becomes.

Throughout our study of pathology we must remember that the changes contemplated are but perversions of the normal. Disease, with its alterations in structure and function, is not an entity from without, not an importation whose existence within the body is passive, but that all morbid processes, while they may arise from causes acting from without,—causes having an existence as a part of the world around us,—are themselves, essentially, but perversions of normal vital activity. The same cells, or their progenitors, active in a morbid process, were the essential elements in the normal life of some tissue of the body. As the result of altered

conditions, the cellular activity has been perverted, and the new line of cell-life is but a change in the manifestations of cellular activity,—not a new, or foreign, or extraneous life carried on within us. The apparent exception to this, in the growth of animal and vegetable parasites within the tissues, is not really an exception; so long as the life of the normal cells is not in any way disturbed, disease does not result; as soon, however, as the foreign elements interfere with the usual course of events, those cells which perform certain functions in a manner which we recognize as normal for the species under observation, assume a new rôle, and manifest their activity along a line foreign to their usual course. We thus see that the diseased tissue is the result of changes in the normal, and the cellular elements present are but modified forms of normal cells.

As will be seen later (Part II), pathology implies a study of (1) etiology—the causes of disease, (2) morbid anatomy—the lesions of disease, (3) the changes in function induced by the disease, and (4) the results which follow the subsidence of the morbid process. The methods of study must, of necessity, vary with the morbid process under consideration. Where any of the lower animals are susceptible to a disease under investigation, for evident reasons, the experimental method offers many advantages. Being able to vary the conditions under which we may induce a disease in an animal, to kill the animal at any period in the development of the morbid process, and to more fully control external conditions, makes this method, in many instances, of the greatest value. Like all our methods for studying disease, the experimental method is open to certain objections: we can not, in all cases, interpret the results, or they may not be fully applicable to man; while this important objection to the method often holds true, the writer does not recall a single instance in which, after prolonged effort, we have not learned something.

In many diseases, all we know has been tediously worked out by the experimental method. Again, many diseases to which man is liable can not be induced in animals, and in such cases the method fails us. It has been urged that the end attained does not justify the suffering induced in the animal experimented upon. Such an objection need not be answered here, since those who hold it can not know of the advances made by the experimental methods of study, and are not in that condition of mental receptivity necessary to appreciate scientific truths. The results attained by experimental study of disease have probably done more to alleviate suffering in the lower animals than in man.

Comparative pathology—the study and comparison of morbid processes in the lower animals and in man—also affords ample opportunity for advance in our knowledge of disease.

In all pathologic study, to attain the best results the statistic method must be used to a certain extent. The collection of a large number of cases with a careful analysis of recorded data can but yield valuable conclusions. The constancy of associated lesions, as, for example, the association of certain nervous and nutritive phenomena with removal or disease of the thyroid gland, often indicate a path for investigation which may terminate in a happy solution of some obscure problem.

The study of diseased organs or tissues postmortem, or after removal from the body, need hardly be mentioned as a most fruitful source of knowledge concerning morbid processes.

Probably more important than any of the preceding, certainly equally important, is a thorough study of etiology, not only by some or all of the methods just indicated, but by accurate observation applied to all cases of a disease, often, if it must be so, irrespective of the possibility of making a subsequent study of the lesions induced.

In addition to the above methods, we can never go amiss by thoroughly studying morbid processes during life. Therein lies the strength of our science. The symptoms of a disease are but expressions of the lesions, the morbid physiology induced by chemic, mechanical, or structural alterations. From symptoms we may infer, in many cases, the character of the tissue changes, or, by studying the alterations in the normal chemistry and structure, we may explain symptoms. He is far at sea who believes the study of pathology begins and ends with the postmortem.

PART I.

TECHNIC.

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TECHNIC.

CHAPTER I.

POSTMORTEM EXAMINATIONS.

I. INSTRUMENTS NEEDED.

One Virchow postmortem knife.
Two strong scalpels.
Two small scalpels, one probe-pointed.

FIG. 1.—COMPLETED POSTMORTEM CASE.
It is convenient to have a leather covering for the case.

One costotome, or, when this can not be obtained, a cartilage knife or a saw may be substituted.
Two dissecting forceps.
One scissors, one blade sharp and one probe-pointed.
One enterotome, or, when this is not available, a small cork

or piece of wood may be pushed over the tip of the sharper pointed blade of the ordinary scissors.

Two long probes,—one should have an eye.

One saw with a well-bellied cutting edge.

One grooved director.

Two large postmortem needles.

Two spools of flaxed thread; one white, one black.

One mallet; the rawhide mallet has the advantage of making but little noise when used on the chisel.

One chisel.

II. PRELIMINARY DATA.

Before beginning the postmortem, it is desirable to know and record the name, age, residence, or, in hospital cases, the ward and bed, sex, color, date and hour of death, date and hour of postmortem, methods of preservation if any have been used, the clinic diagnosis, the name and residence of the physician, if any, who last attended the case, and, if possible, his presence at the postmortem.

In medicolegal cases the body should be identified. If the time at which death took place is not known, it may be approximated by the postmortem evidences.

III. THE POSTMORTEM.

In order that the record of a postmortem may be perfect, it is absolutely necessary to follow a definite method in each case. If circumstances demand a variation from this routine method, the *reason for varying should constitute a part of the record.* The following presents nothing original, and is the method adopted by the writer:

(A) The Date and Hour of the Postmortem.

(B) External Examination of the Body.

(*a*) *Is the body dead?* The following observations should be made, and recorded as a part of the postmortem notes, as they cover not only the signs of death, but constitute a part

of the evidence of diseased conditions: (1) Examine for evidence of respiration and circulation. (2) Look for opacity of the cornea, loss of sensibility in the conjunctiva, pupillary reaction, which may, in doubtful cases, be tested by atropin or eserin; if the eyes are sunken, with wrinkled tunics, the evidence is clear. (3) Pallor of the body may or may not be present, and while valuable as a sign of death, it may be found in the living during swooning, the algid state of ague, collapse, etc. (4) Cooling of the body to the temperature of the surrounding medium (*algor mortis*) occurs in from fifteen to twenty-four hours. Children's, and old and lean bodies, cool quite rapidly, while fat, young, and middle-aged bodies retain the heat much longer. The bodies of persons dying from suffocation, electricity, tetanus, and yellow fever very slowly yield their heat. (5) *Cadaveric rigidity*, or *rigor mortis*, occurs at a varying interval after death. It may become manifest but a few minutes after death, or it may be delayed eighteen or twenty hours; usually, it develops simultaneously with the loss of body heat. The duration of rigor mortis is extremely variable, lasting in some instances but a few moments; in other cases, hours, days, or even weeks. (6) *Cadaveric lividity* (the cadaveric blotches called *livores mortis*) and *suggillation* are terms applied to the livid or violet-colored discoloration which is seen usually several hours after death. It becomes apparent in the most dependent portion of the body, and is the result of blood gravitating into the capillaries. (7) *Putrefaction* is an indubitable sign of death. The time at which it becomes manifest varies greatly, and is dependent upon the condition of the body, the surrounding media, and the cause of death. (8) Experimentally, we may infer that the body before us is dead by injecting ammonia water under the skin; in death such a procedure leaves no mark, but in simulated death it occasions a dark spot. A dead body can not be blistered.

(*b*) *General Considerations.*—The amount of adipose tissue,

the muscular development, and the nutrition of the body, should be carefully noted, and the record completed or verified as the internal examination proceeds. In case the body has not been identified, an elaborate description should be made for the purpose of further identification ; the height, weight, measurement of chest, limbs, hands and feet, color of eyes and hair, and of the latter some should be preserved. A careful survey of the mouth as to dental peculiarities, absence of teeth, filled or irregular teeth, or, better, a dental impression taken in wax or plaster. If false teeth are present, they should be removed as possible aids to future identification. Abnormalities, malformations, marks of any kind, should be noted, and, where possible, a photograph be obtained.

(*c*) *Evidence of Violence or Disease.*—*Ecchymoses* should be carefully described as to size, shape, and position. This form of discoloration may be distinguished from *suggillation* in that it does not disappear on pressure, and if an incision be made into it bloody fluid will escape, or a clot may be discovered in the subcutaneous tissue. All abrasions, eruptions, bed sores, ulcers, cicatrices, wounds, edema, pigmentations in the skin and mucous membranes must be accurately described, and their positions carefully recorded. Fractures and dislocations must be closely observed, and their character and the parts involved noted. The external orifices of the body should be examined, and their condition and contents noted ; *e. g.*, mouth and nose for foreign bodies, evidences of corrosive poisoning, etc. ; in the female, the breasts, abdomen, and external genitals should be examined for evidences of disease, violence, or physiologic processes, such as menstruation, recent delivery, or evidences of past gestation, as shown by the mammæ, abdomen (linea albicantis), or external genitals. In the male, look for evidence of malformation of the sexual organs, or venereal disease, also seminal stains. Examine the anus for fissures, inflammation, fistulæ, morbid growths, cicatrices, etc. Exam-

ine the hernial outlets for evidences of rupture. If the body is that of an infant, examine the fontanels and sutures, and note the various diameters of the skull. Measure the body and examine the umbilical cord. In the male the scrotum should be examined to determine if the testicles have descended; note, also, the presence or absence of vernix caseosa. Carefully examine the epiphyses, and especially that of the lower extremity of the femur.

(C) Internal Examination of the Body.

The large Virchow knife is used for most of the incisions; it is grasped firmly in the hand by the thumb, middle, ring, and little fingers, while the index finger rests upon, or at the side of, the blade. Cuts are made with a drawing movement, the shoulder and elbow joints acting as centers, the wrist and

FIG. 2.—MODIFIED VIRCHOW POSTMORTEM KNIFE.
Twenty-four cm. long, of which 9.5 cm. is cutting edge.

fingers rigid. In ordinary dissection a scalpel is held like a pen, motion being at the joints of the fingers and wrist—a process entirely too tiresome and slow for postmortem work except where very delicate dissections are to be made.

The body rests firmly upon the back, and the operator, if right-handed, stands upon the right of the cadaver. To expose the abdominal and thoracic cavities, an incision should be carried from the lower border of the thyroid cartilage, or from the interclavicular notch, to the symphysis pubis, making a sharp semicircular turn to the left at the umbilicus in order to avoid injury to the remains of fetal organs at that point. Over the abdomen, the first incision should pass through the skin and subcutaneous tissue; then carefully cut through the abdominal wall immediately below the ensiform cartilage; in-

sert two fingers of the left hand, drawing the abdominal wall

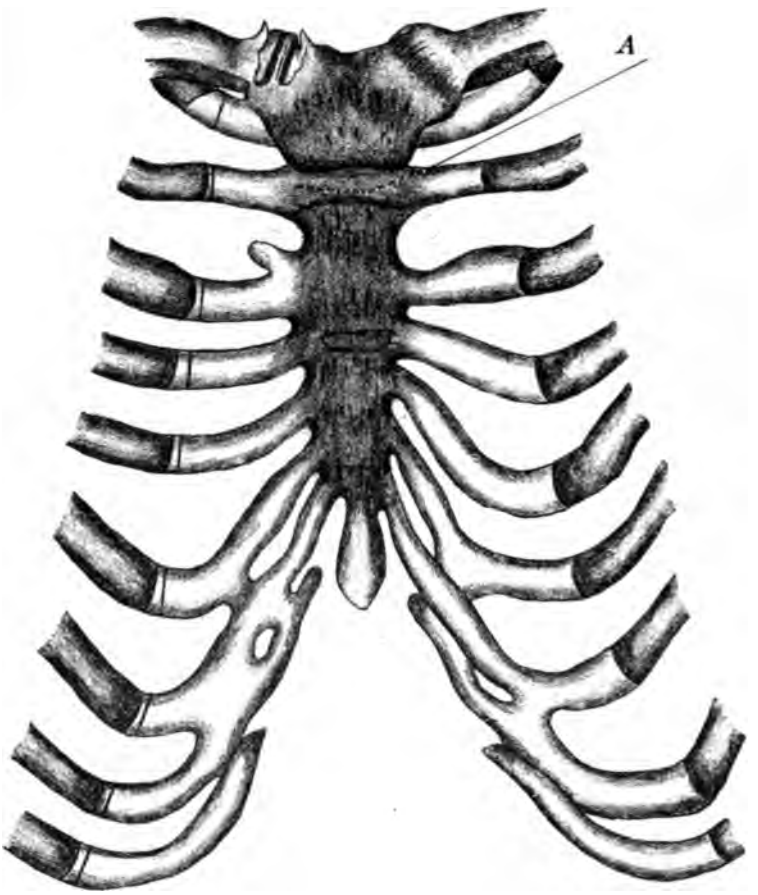

FIG. 3.—THE STERNUM, COSTAL CARTILAGES, AND ARTICULATION OF THE CLAVICLE, AS EXPOSED AFTER TURNING BACK THE SOFT PARTS.—(*Modified from Virchow.*)

On the left is shown the line of incisions made through the cartilages from below upward, if a costotome be used; from above downward if a knife or saw is employed, and also the incision necessary for disarticulating the clavicle. Where it is not desirable to disarticulate the clavicle, the manubrium is separated from the gladiolus at point *A*, the incision being made from behind.

upward; continue the incision, the fingers being used as a

guide to the knife. Note the amount and color of the subcutaneous fat in the abdominal wall, its consistency, and the presence or absence of edema. Examine the muscles for pallor, hyaline spots, degenerative changes (such as occur in typhoid fever), and small white ovoid bodies, encysted trichinæ. Dissect the tissue from the chest walls as far back as the junction of the costal cartilages with the ribs; then make strong traction on the abdominal walls to break up the rigor mortis. After breaking up the rigor mortis, the muscles can be further incised, and examined for evidences of bruises, inflammation and suppuration, and suspicious portions removed for microscopic study.

Abdominal Cavity.—First note the relative position and color of the liver, stomach, and intestines; and also the relations of the viscera to the costal and ensiform cartilages. The examination of the cavity is not of the organs individually, but of their relation to one another and to the walls; also examine the serous membrane,—the peritoneum. A careful search should be made for adhesions and other evidences of inflammation, recent or old, and for thickening and opacity of the serous membrane. The amount and character of any fluid in the cavity must be noted, and, if in excess, or abnormal in character, the source or cause of the morbid condition must be sought. The color of the liver should be observed before those changes incident to the oxidation of the blood occur. Carefully search for perforations of the bowel, stomach, bladder, or gall-bladder whenever the fluid in the cavity is abnormal. Accurately note the position of the diaphragm; ordinarily, on the right side it ascends as high as the fourth rib, or interspace, and on the left to the fifth rib. Remove any fluid present in the cavity before going to the thorax, as fluids in the abdominal cavity would flow into the thoracic cavity and thereby complicate the examination.

Thoracic Cavity.—With a heavy knife, or costotome (or, in the absence of the latter, where the cartilages are calcareous,

a saw may be used), sever the costal cartilages close to the ribs, care being exercised not to injure the tissues beneath. Divide the attachment of the diaphragm, raise the sternum, and dissect off the attached tissue, taking care to direct the edge of the knife toward the bone in order to avoid injury to the

FIG. 4.—COSTOTOME.

pericardium or other intrathoracic tissues. Cut the ligaments which bind the clavicle to the sternum, divide the sternal attachment of the sterno-cleido-mastoid muscle, and pull the breastplate to one side. In a cadaver in which the section of the thorax has been made as just directed, the shoulders,

FIG. 5.—SAW.
A large, firm handle is wanted, with good pistol grip.

having lost the support of the clavicle through their sternal attachment, collapse together, making the chest appear very much distorted. To avoid this, in cases where the body is to be viewed, it is suggested that the manubrium and gladiolus be disjointed, which may be accomplished by drawing the edge of the knife across the under surface of the articulation

of the manubrium and gladiolus and raising the lower segment of the sternum.

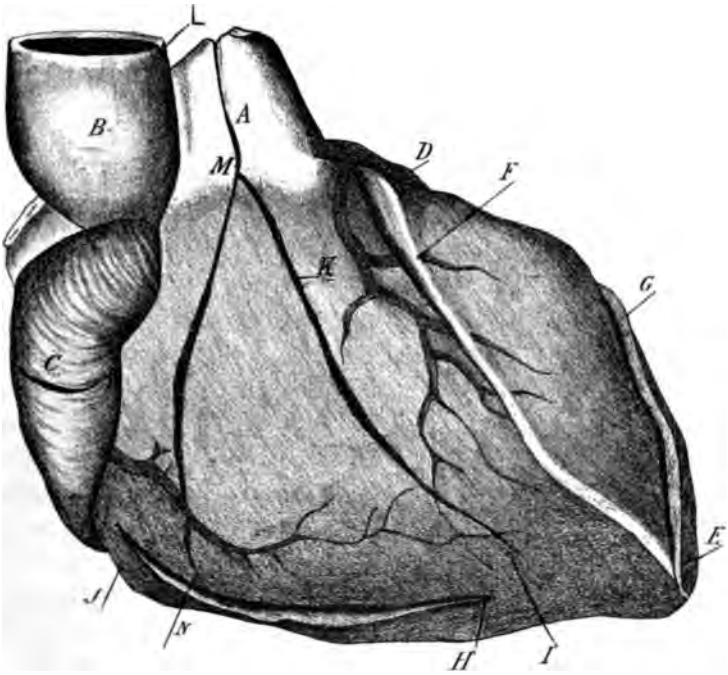

FIG. 6.—HEART SHOWING THE LINES FOR INCISIONS IN THE PRELIMINARY EXAMINATION AND FINAL SECTION FULLY EXPOSING THE VALVES.—(*After Virchow.*)

A. Pulmonary artery. B. Aorta. C. Right auricle. The incision M to N is that advised by Virchow. The one preferred by the writer is from K to I, for the preliminary opening of the right ventricle. The preliminary opening of the right auricle is made at C. The preliminary opening of the left auricle is made at D. The preliminary opening of the left ventricle is made at F to E. After the heart is removed the incision made at C is carried out through the vena cava; the incision from K to I is carried through the pulmonary artery between the letters M and A, and below is carried around by H to J. The incision M, N, is not made. The incision F to E, in the left ventricle, is carried around behind the pulmonary artery A and comes out in the aorta at L. From the lower portion, at E, the incision is carried upward to about where the letter G is shown; this permits the flap to be turned back so that the mitral valve may be examined; the incision made may then be carried through the mitral orifice.

Examine the pleuræ for evidences of inflammation, either remote or recent; note presence or absence of fluid, also its

quantity and character, as in the peritoneum. Fluid in each pleura should be measured and removed so as to prevent its flowing into the pericardium, or, in case the pericardium contains much fluid and any escape into the pleura, its quantity may be accurately estimated. Adhesions should be looked for and described. The pericardium should now be opened by an incision extending from base to apex in a line parallel to the

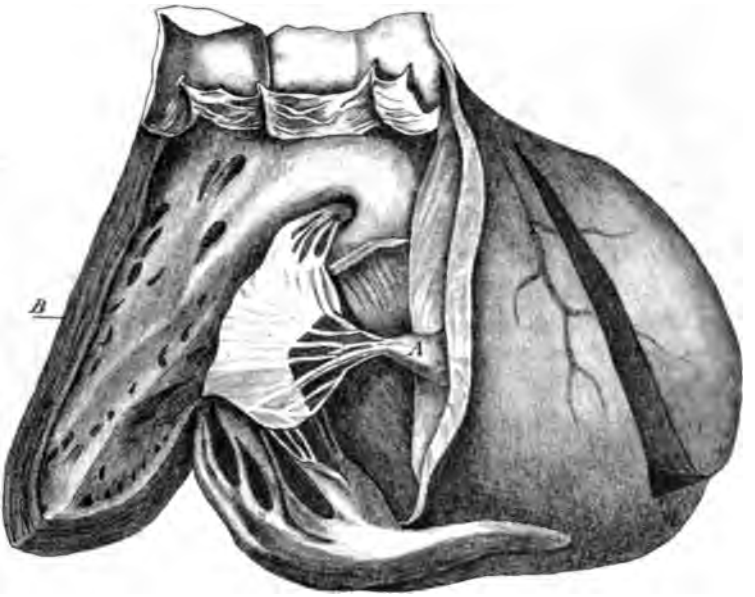

FIG. 7.—HEART SHOWING THE INTERIOR OF THE RIGHT VENTRICLE AND PULMONARY ARTERY.—(*After Virchow.*)

If the incision, *M* to *I*, Fig. 6, be made, as advised by the writer, the papillary muscle, *A*, will be carried over with the ventricular wall, *B*, thereby better exposing the auriculoventricular orifice.

long axis of the heart. Examine the layers of the pericardium for evidences of inflammation, and look carefully for adhesions, particularly about the great blood-vessels. Measure the pericardial fluid and note its character. The heart should now be examined. Note the condition of contraction or relaxation of

the heart's wall; open the heart *in situ;* raise the organ by its apex, pass the fingers of the left hand under the organ, and so grasp it that the thumb and first finger will close the auriculoventricular orifice of the right side, and then make an incision into the auricle between the venæ cavæ. Examine and

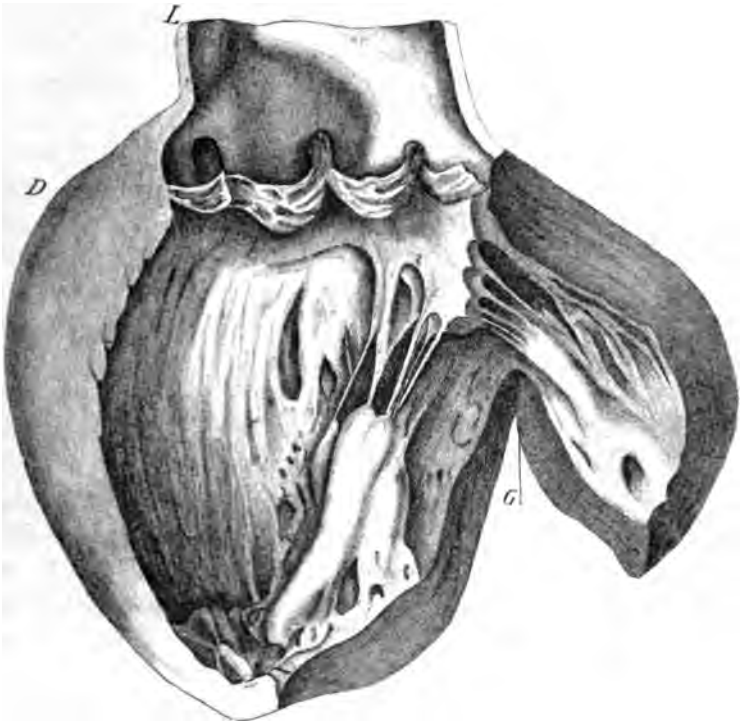

FIG. 8.—HEART WITH THE LEFT VENTRICLE LAID OPEN, SHOWING THE AORTIC CUSPS AND THE VENTRICULAR ASPECT OF THE MITRAL VALVE.—(*After Virchow.*)
The letters have the same significance as in Fig. 6.

note character of contents; without relaxing the grasp on the auriculoventricular orifice, open the right ventricle by an incision in line with the pulmonary artery and close to the ventricular septum; insert the index finger of right hand and examine the contents. The left heart is opened by grasping

it as in opening the right. The auricle is incised near the appendix and immediately above the auriculoventricular septum, and its contents noted. The left ventricle is opened by an incision almost parallel to the opening made in the right ventricle, but on the opposite side of the septum, and the incision is directed toward the aorta. The presence or absence of blood or clots in the left ventricle must be carefully noted. Examine the great vessels as to abnormality, aneurysm, or other disease discernible externally. Remove the heart, dividing the great vessels from below upward, severing the aorta last. Test the valves as to competency, being sure to wash out all clots before making the test. Measure the valvular orifices. Enlarge the incisions already made so as to be able to examine the endocardium in detail. Carry the incision in the right auricle out through the two cavæ; prolong the incision in the right ventricle through the pulmonary artery and the incision in the left ventricle through the aorta. The left auricle is opened by continuing the incision already made into the pulmonary vein. Note any vegetations on the valves, thickenings or opacity of the endocardium; examine closely the condition of the foramen ovale. State the general appearance of the cardiac muscle.

Examine coronary arteries by passing a director into each in turn, and, with knife or scissors, opening the artery as far as possible. Weigh the heart.

Both lungs may be removed at once. Incise the great vessels as they pass out of the thorax; cut through the trachea, being careful not to injure the esophagus. Gentle protracted traction will strip the organs from the tissue behind, bringing forward with the pericardium the aorta, which must be severed at the diaphragm. If it is desired to leave the aorta, this can easily be done by separating it from the pericardial attachments before delivering the lungs. Where removed singly, the left lung is removed first. Note the general appearance,

color, and condition of the lung. Incise and examine carefully, noting any pathologic change which may be present. Lay open and dissect down the bronchi, and carefully examine

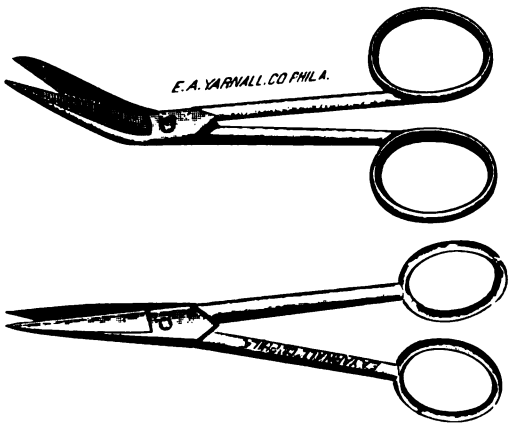

FIG. 9.—SCISSORS.

Those shown in the upper cut will be most useful, particularly if the blade shown in the cut as having the sharper point be slightly probe-pointed.

their condition, a sharp lookout being maintained for the presence of foreign bodies. Note the appearance of the peribronchial glands. Weigh each lung separately. Examine larynx, trachea, bronchi, and thymus and thyroid glands.

FIG. 10.—GROOVED DIRECTOR.

Useful for opening arteries, tracing sinuses, ducts, etc.

ABDOMINAL VISCERA.—The *spleen* is now removed. Its general appearance described, make one long incision through the back of the organ down to the hilus. Note color and consistence of parenchyma, prominence of the Malpighian bodies, and stroma. Weigh the organ.

The Kidneys.—Determine that both are in their normal positions, if possible. The left suprarenal body and left kidney are next examined. Raise the kidney from its normal position, note condition of blood-vessels and incise them; examine ureter and sever it. Hold the kidney in the left hand, with the pelvis directed toward the palm, and with one sweep of a sharp knife incise, from the cortex to the pelvis, in the long axis of the organ. On section, note consistency, color, the relative proportion of cortex and pyramid (normal cortex equals one-half the pyramid); the condition of capsule, whether thickened, tense or flaccid, or adherent to cortex; also note appearance of stripped surface of cortex, whether smooth or rough, etc. Examine pelvis of kidney, and weigh the organ. The same process is repeated upon the opposite side.

FIG. 11.—LONG, THIN BRAIN KNIFE; OF VALUE FOR INCISING ORGANS.

Originally designed for brain dissection, and mostly used for opening the kidneys, liver, spleen, tumors, etc. It is long and thin, and if properly used leaves a clean, smooth surface for inspection. The cutting edge of the instrument should be not less than 16 cm.

Examine bladder and internal genitals. If urine be present in the bladder, its quantity should be noted, and it should be preserved for future examination. The left semilunar ganglion is examined and any firmness or inflammatory signs noted. The ganglion should be preserved for microscopic examination. The corresponding organ of the right side is next in order of examination.

The Stomach and Duodenum.—In cases where poisoning is suspected, ligatures are tied at the cardiac extremity of the stomach and the upper end of the duodenum, and the organ removed, placed in a clean jar, and sent to the chemist, without opening, that the contents may be carefully examined. In case it is decided to open the duodenum and stomach *in situ*,

as is best when the question of poisoning does not enter into the case, make an incision along the anterior surface of the duodenum and greater curvature of the stomach. Examine contents, condition, and appearance of mucous membrane. Foreign bodies are frequently met with in the stomach. Determine if the bile duct be patulous by pressing upon the

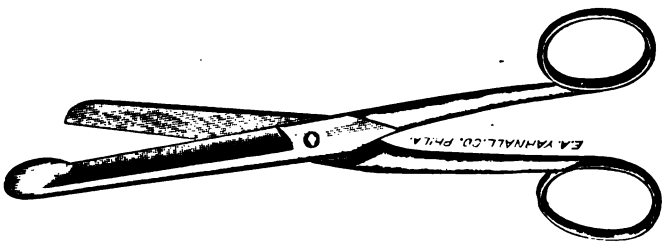

FIG. 12.—ENTEROTOME.

Useful for opening stomach, duodenum, intestines, etc. Not uncommonly the blunt-pointed lower blade is so made that it forms a tooth, like the barb on a fish-hook, and when introduced can not be withdrawn. Never purchase such a hook-pointed enterotome.

gall-bladder and watching for the escape of bile. Open the ductus communis choledochus and examine mucous membrane.

The vena cava is now opened and the condition and appearance of the blood noted.

The liver may now be removed; its shape, contour, color,

FIG. 13.—PROBES.

These should be at least 15 or 20 cm. long. One should be very slender.

and any deformities of the lobes noted. The anterior margin examined and condition noted. On section, the firmness or resistance should be noted; also the color, whether uniform or mottled, and whether or not bile staining be present. Weigh the organ.

The pancreas may now be removed and any peculiarity or change carefully noted.

The œsophagus should now be examined and *the intestines* removed. The latter should be carefully washed and opened, and then examined for inflammation, ulcers, cicatrices, perforations, constrictions, etc. It is probably best to open the intestines before washing them out, in order to more accurately determine their contents, examine for animal parasites, locate foreign bodies, etc. In cases of suspected poisoning, the intestines should be sent, unopened and in a clean jar, to the chemist.

The *thoracic duct* should now be traced and the *receptaculum chyli* examined, also the *mesenteric and retroperitoneal glands.*

The *aorta* and its branches may now be examined in detail.

THE HEAD.—Insert the scalpel, with its back toward the skull, just behind one ear, and carry an incision across the vertex, cutting from within outward. If the knife be not too sharp, the hair may be parted and thrown backward and forward as the hand and knife are withdrawn. The incision should be far enough back to be invisible from the front when closed. The scalp is reflected forward and backward from this incision as low as the superciliary ridge in front and the occipital protuberance behind.

In many cases great care must be used to avoid a tear at or around the ear, as tension is produced by pulling the anterior and posterior scalp flaps down; to avoid this unsightly tear, which may run down in front of the ear, insert the knife under the skin, in the incision already made, just behind the ear, and dissect the skin free from the deeper structures behind and in front of the ear. The scalp flaps, as already described, do not include the temporal fascia or muscle, which is now cut through and reflected in the line of the contemplated saw cut. Sawing is greatly facilitated by having all soft tissue free of the line of the contemplated cut, as the soft parts clog the

teeth of the saw. When the skull-cap is replaced, the fascia and the muscles may be sewed together, thereby securing the bone in place—a matter of great importance in private post-

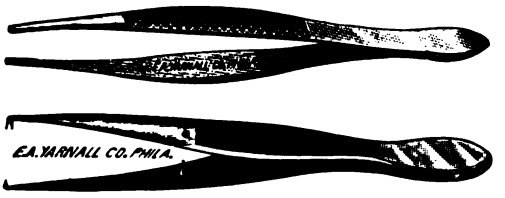

FIG. 14.—DISSECTING FORCEPS.

One of these should be toothed. These will be needed in the finer dissections, as in tracing the hepatic duct, portal vein, and receptaculum chyli.

mortems where the body is to be exposed at a funeral or to friends.

Inspect the skull for evidence of injury or disease. In opening the skull, there are three methods of procedure: one should never be used, one may be used in a few cases, and one is applicable in the vast majority of instances. (1) The

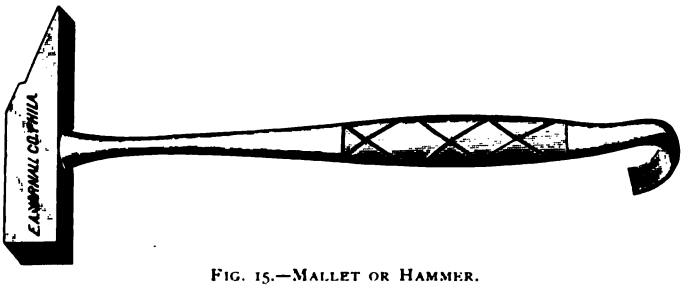

FIG. 15.—MALLET OR HAMMER.

"undertaker's cut" consists in sawing across the forehead just back of the hair line, from one temporal fossa to the other, and carrying a second saw cut around the posterior base, parallel with the base line, joining the anterior cut in each temple. This method does not permit of satisfactory removal of the

brain. (2) The second method should always be used in medicolegal cases, and wherever the question of fracture may arise. It does not demand the use of a chisel, and affords abundant opportunity for examining the skull's interior. A circumferential line is drawn around the base of the skull, on a level with the superciliary ridge in front and the occipital protuberance posteriorly, and the skull sawn through at this line. (3) The third method, and the one most commonly employed, consists of a V-shaped incision; as viewed laterally, the anterior arm of the V is parallel with the base of the skull,

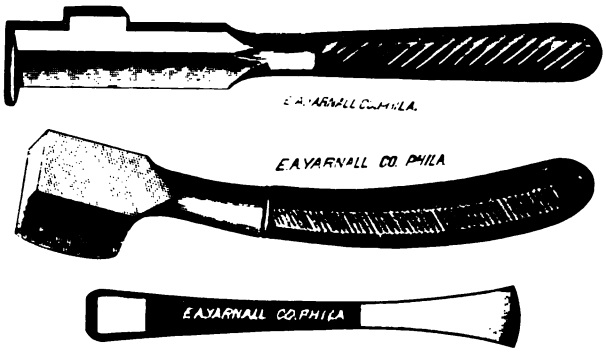

FIG. 16.—CHISELS.
If only one is to be purchased, the lowest one will be of most use.

on a level with the superciliary ridge, and extends backward as far as ½ of an inch behind the external auditory meatus. The other arm of the incision passes obliquely across the vertex just back of the incision already made in the scalp. It may be necessary to break out the angles of the saw cut with a chisel; care must be used not to mutilate the ear in making the saw cut. The advantage of this incision lies in the easily adjusted calvaria, the wedge-shaped cap being readily replaced and secured in position, so that no external evidence of the postmortem will be visible when the scalp is secured in place.

Inspect the interior of the calvaria for evidence of injury

or disease, noting its thickness and the condition of the diploe and of the external and internal tables. The dura may be removed, or, rather, reflected back, by incising it along the lower saw cut and detaching the falx cerebri from the crista galli.

Inspect the surface of the brain for superficial injuries or disease, but make no incision into it. It may here be necessary to note the relation of brain landmarks to the skull, fixed points of the latter being selected for the comparison.

The brain is next to be removed, beginning in front by carefully raising it from the base, being careful to raise the olfactory bulbs with the hemispheres; still carefully elevating

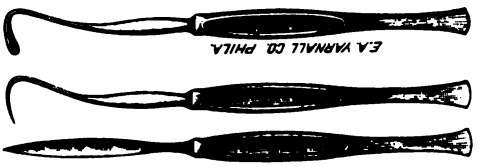

FIG. 17.—SCALPEL WITH BLADE SHAPED SOMEWHAT LIKE A BISTOURY.
Useful in removing the brain and spinal cord. The aneurysm needle and tenaculum shown above are useful at times, but one can get along without them.

the hemispheres, sever the nerves as they pass out of the skull, those in front first, and then in order as they appear. When the tentorium is reached, detach it from the temporal bone and follow the base, severing the nerves as they find exit from the posterior fossa; lastly, pass a long, slender-bladed knife along the basilar process of the occipital bone, and down into the spinal canal, cutting the cord as low as possible. The entire brain can then be easily removed. Complete the examination of the interior of the skull, noting the condition of the bone, blood-vessels, sinuses, etc. The posterior part of the orbit and the eyeball may be examined by chiseling the roof; in the same way examine the frontal, sphenoid, mastoid, and ethmoid sinuses and the internal ear.

The brain should be hardened before dissection; if this can not be done, immediate examination may be made as follows: Make a careful examination of the meninges, and note the color, consistence, etc., of the external surfaces, including the base; examine the blood-vessels at the base, tracing them into the brain tissue. An incision is made on each side, just over the corpus callosum, into the lateral ventricles, and continued backward and forward, that they may be carefully inspected; the amount and character of the fluid present is noted. The lateral ventricles are joined by an incision through the fornix, exposing the tissues beneath. Search for hemorrhages, areas of softening, tumors, inflammation, abscesses, etc. Lateral incisions are now made in the cortex from the ventricle outward, so as to note the condition of the cerebral substance; the incisions should be parallel, not over one centimeter apart, and the membranes should not be cut through, as they will retain the cut parts in position. The brain is then turned over, and the tissue of the base examined by transverse incisions through the medulla, cerebellum, etc., examining for such changes as above noted. Weigh the brain.

The Spinal Cord.—The body is turned upon the abdomen, and blocks so arranged as to arch the vertebral column. An incision is then made through the skin, over the spinous processes, and the muscles, fasciæ, etc., detached from the vertebræ so as to expose the laminæ on both sides. These are then sawn through, the saw being held parallel with the spinous processes, and the cut made near where the laminæ join the pedicle. These are sawn through from the second vertebra to the sacrum and removed, the chisel or bone-cutting forceps being used as aids if necessary. Inspect the meninges and remove these with the cord, carefully detaching, with a sharp knife, the nerve roots as they pass out of the canal. The lower end of the cord, with its membranes, is first detached, and the removal continued from below upward.

During the removal of the cord, whatever traction may be necessary should be made on the meninges only, and traction on, or crushing of, the crod should be carefully avoided. Lay

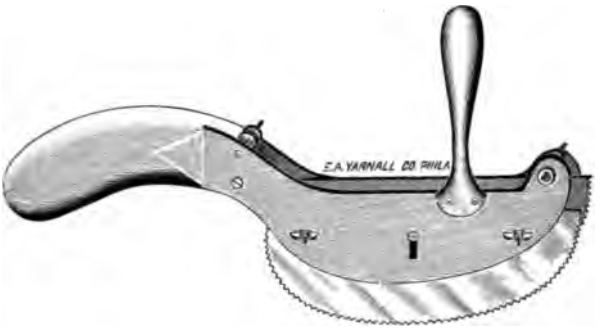

FIG. 18.—DOUBLE SAW FOR SAWING THROUGH THE LAMINÆ OF BOTH SIDES AT ONCE. It saves time and labor, but equally good work can be done without it.

open the meninges and examine the cord by making transverse incisions every centimeter.

In considering organs, a definite field or plan should be adopted. Of course this will be quite often varied, but it has the advantage of occupying no more time than any other way,

FIG. 19.—BONE-CUTTING FORCEPS.
These are not absolutely essential, but will be convenient. They should be long—not less than 15 cm.

and assures a systematic record which makes all postmortems comparable. The following is advised, although each worker will probably acquire a routine of his own :

(1) *Malposition*, and, if out of place, is the malposition con-

genital or acquired, and what influence has it had on the position or function of other organs; *e. g.*, a misplaced right kidney may press upon the duodenum or bile duct or both. After removal it is too late to determine such facts, which may be of the highest importance in explaining symptoms. (2) *Malformations.* (3) *Make measurements* of the organ and *weigh* it; as the organ can only be weighed after removal, and as the removal severs its connection with the body, note must be made of *color, consistence, density, shape,*—the latter being outlined when the measurements are made,—and a full *description of its external appearance;* at the time of severing its attachments the *fullness of the blood-vessels*, the presence or absence of *edema*, and, if it possesses a duct, the condition and contents of that structure must be recorded. These studies enable one, to a certain extent, to record the presence or absence of the following points, which come next in order. (4) *Atrophy*, including hypoplasia or aplasia. (5) *Hypertrophy*, including *hyperplasia.* (6) *Infiltration.* (7) *Degeneration.* (8) *Inflammations*, including acute *infections.* (9) *Lesions of systems:* (*a*) *Vascular;* (*b*) *Lymphatic;* (*c*) *Nervous.* (10) *Chronic infections.* (11) *Tumors.* (12) *Parasites.* If the steps indicated be followed, but little will be overlooked. If a bacteriologic examination is to be made, the cultures should be made as soon as the organ is reached.* As soon as an organ is incised, pieces should be removed and fixed for microscopic study, and the records completed after the microscopic examination is finished.

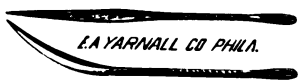

FIG. 20.—POSTMORTEM NEEDLES. These should be 8 to 15 cm. long and correspondingly heavy.

PRESERVATION OF TISSUES.

For preserving gross specimens alcohol is most commonly

* The method for securing cultures from organs postmortem is described in the section on bacteriology.

used. The tissue is washed in running water for a few hours to remove adhering blood, and is placed in 50 per cent. alcohol; at the end of two to four weeks the alcohol should be replaced by 60 per cent. alcohol, in which the tissue may be preserved indefinitely. If a snowy whiteness is desired, a mixture of glycerin *one* part, water *three* parts, and alcohol *five* parts will be found useful for the final preservative. Specimens which have been preserved in glycerin mixtures are of little value for microscopic purposes, as they can be frozen, imbedded, or infiltrated only with the greatest care, and usually with unsatisfactory results. Of late, formalin * has come into great demand for the hardening and preservation of tissues. A ten per cent. solution in water will be found convenient, or the following when more time is available: The specimen to be preserved is lightly washed in water only, to remove adhering blood. It is then placed for ninety-six hours in—

Formalin,	750 c.c.
Nitrate of potassium,	10 gm.
Acetate of potassium,	30 gm.
Water,	1 liter.

Wash thoroughly in water and place in 80 per cent. alcohol for twenty-four hours, and permanently preserve in a mixture composed of alcohol eight parts and glycerin one part. This mixture preserves the color fairly well, and after a time the specimen can be handled without injury to the hands.

Organs or specimens not too large (one kilo) can be preserved in formalin vapor by placing the material to be preserved on a bed of cotton in an air-tight jar, previously moistening the

* Formalin is a proprietary compound composed of 40 volumes of formaldehyd dissolved in one of water. The original formalin was expensive, but equally efficient solutions, under other names, as *formalose*, can be obtained now at a price making preservation by this method cheaper than with alcohol.

cotton with pure formalin, and for the first few days keeping the specimen covered by filter-paper moistened with formalin.

In hardening of the brain tissue, formalin has superseded Müller's fluid for the gross specimen, but for histologic research there is nothing which can supplant the latter at present. It darkens the tissues, and thus alters their macroscopic appearance.

Small cysts, such as those of the echinococcus, are best preserved in a ten per cent. solution of chloral in water.

QUESTIONS.

(1) What instruments will be needed for postmortem examination? (2) What preliminary data should be made a part of the record? (3) What are the signs of death? (4) What information is sought by the external examination? (5) What is an ecchymosis, and how would you differentiate from suggillation? (6) Give method for opening the abdominal cavity and for the incision through the soft parts of the thoracic cavity. (7) What information is sought in the preliminary examination of the abdominal cavity? (8) How open the thoracic cavity? (9) Give order of examination of thoracic contents. (10) How open the pericardium? (11) What is the first point to determine in the examination of the heart? (12) How examine the heart *in situ*? (13) Describe, in detail, the proper method of opening the heart cavities. (14) How remove the heart? (15) How complete the dissection of the heart? (16) Describe the removal of the lung. (17) How examine the bronchi? (18) What other organs are now examined in the thoracic cavity? (19) Give the order in which the organs of the abdominal cavity are examined. (20) Give method of examining the spleen. (21) What information should be obtained before removing the kidneys? (22) What organ is removed with the kidney? (23) What point must be determined before severing the blood-vessels and ureter? (24) How incise a kidney for examination? (25) What organ is examined after the kidneys? (26) What organ is examined after the genitalia? (27) Under what conditions would you open the stomach before its removal, and why might you desire to remove it before opening? (28) How examine the bile duct? (29) How examine the liver? (30) How make the incision through the soft parts for examining the head? (31) What information is sought by the external examination of the skull? (32) Give in detail

the methods for removing the skull-cap, and reasons for selecting one or another method. (33) Describe the superficial examination of the brain and the steps necessary for its removal. (34) Describe the internal examination of the skull. (35) Describe the dissection of the brain. (36) How open the spinal canal and remove the cord? (37) Give the order to be followed as nearly as possible in the examination of any organ. (38) What general information should be obtained during the examination of any organ? (39) Give recommended methods for preserving tissues.

CHAPTER II.

HISTOLOGIC METHODS.*

Morbid Histology.—Technic.—Sections of the fresh tissue may be cut free-hand, or by means of Valentine's knife, which consists of two parallel knife-blades of the utmost sharpness separated from each other by a small aperture just as wide as the section is to be thick. The method is unsatisfactory, and is rarely used. Fresh tissue may be cut by freezing, as will be directed later. Since the publication of the first edition of these notes, extended experience has convinced me of the necessity of thoroughly fixing all tissues before attempting to section them. By *killing* or *fixing* is meant the destruction of all metabolic processes and securing the tissue in a permanent condition just as it was during life, retaining the cell pictures as perfectly as possible. For general work three methods are advised:

(*a*) Chromo-aceto-osmic acid (Flemming). For this solution keep on hand the following stock solutions, and make up for use as wanted in the proportion given:

Stock solutions to be kept on hand.	*Quantity needed to make up above solution.*
1 per cent. aq. sol. chromic acid,	25 volumes.
1 " " " " osmic "	10 "
1 " " " " acetic "	10 "
Water,	55 "

* No attempt can be made in such a work as this to go into the subject of histologic technic with elaborate detail. A few methods can be taught, it is believed, thoroughly, but for further detail as to special methods the student had best familiarize himself with that best of all books for the worker with the microscope, "The Microtomist's Vade-mecum," by Arthur Bolles Lee. For description of microscope used in pathologic histology see next chapter.

All the water used in making the stock solutions or the final mixture must be distilled, and all containers chemically clean and dust free.

Fixation of small pieces will be complete in from one-half to two hours, although a longer time may do no injury. Over a few hours, however, is likely to make the tissues brittle. After fixing, wash thoroughly in water.

(*b*) Platino-aceto-osmic mixture (Hermann). Like the above, it is best freshly prepared :

Stock solutions to be kept on hand.	*Quantity needed to make up above solution.*
1 per cent. aq. sol. platinic chlorid, ...	15 volumes.
2 " " " " osmic acid, ...	2 "
Glacial acetic acid, ...	1 "

This solution is used as already directed for Flemming's solution.

(*c*) The most useful fixing agent for general use is corrosive sublimate. The solution keeps well and fixes thoroughly, although for pure cell study the foregoing are probably better. The solution is prepared by dissolving 125 gm. of corrosive sublimate in a liter of 0.5 per cent. solution of sodium chlorid in water. The solution of the corrosive sublimate being effected in the boiling salt solution, on cooling crystals of corrosive sublimate are thrown down, but are again taken up as the solution is used over. Small pieces of tissue fix in this solution in from one-half to two hours. The used solution is filtered back into the stock solution, and the tissue washed in water or, what is better, 70 per cent. alcohol. A little experience soon enables one to infer when the stock solution has become exhausted. By reason of its convenience, keeping qualities, cheapness, and the simplicity of the technic, it is most used.

In fixing by any of the above methods, the tissue should be in small pieces, not larger than 0.5 to 1 cm. cube. The quan-

tity of the fluid used should be abundant, and exceed several times the volume of the tissue to be fixed.

For the preparation of tissue containing nerves, or the central nervous system, nothing is more generally used than bichromate of potassium. It is used in two to five per cent. aqueous solution or as Müller's fluid:

Müller's Fluid.

Bichromate of potassium,	2 parts.
Sulphate of sodium,	1 part.
Water,	100 parts.

Or—

Erlicki's Solution.

Bichromate of potassium,	2.5 parts.
Sulphate of copper,	1.0 part.
Water,	100.0 parts.

The latter hardens much more rapidly; a spinal cord may be hardened in two weeks by this mixture, while by Müller's fluid as many months would be necessary. As the penetration of neither of the above is rapid, nerve tissue placed in them should be freely incised to aid penetration, a spinal cord being cut transversely every centimeter. As soon as the fluid becomes dark or cloudy it should be changed, and the quantity should always be several times the bulk of the tissue. After hardening is completed, the tissue should be thoroughly washed in water before transferring to alcohol.

SECTION CUTTING.

Infiltration Methods.

(1) *Paraffin.*—After fixing and washing as already directed, the tissue to be infiltrated is dehydrated by passing through alcohols of increasing strength—70 per cent., twenty-four hours; 80 per cent., twenty-four hours; 90 per cent., twenty-four hours; absolute, twenty-four hours. As alcohol does not mix with paraffin it must be displaced by some agent

which will dissolve paraffin. For this purpose numerous reagents have been used, such as chloroform, turpentine, xylol, toluol, benzol, cedar oil, and many allied bodies. Many of these alter the tissues, and probably all of them do slightly, but the least objectionable is cedar oil. From absolute alcohol the tissue is carried into the clearing agent, preferably cedar oil, and, to make the change gradual, the cedar oil is diluted with an equal part of absolute alcohol; after twenty-four hours' treatment in this mixture it is transferred to pure cedar oil for twenty-four hours, and then to paraffin, which in summer has a melting-point of 50° C., or in winter 45° C. The paraffin must be kept as near the melting-point as possible by means of a paraffin oven and thermoregulator. After twenty-four hours the tissue is transferred to fresh paraffin at the same melting-point, and kept twenty-four hours. The gentle heat continuously applied displaces the cedar oil and permits the paraffin to infiltrate the interstices of the tissues. A wooden block, about two cm. cube, has one end warmed over a Bunsen burner and dipped in the melted paraffin. It is then wrapped with a strip of paper four cm. wide, so that the paper projecting from the end of the block (which has been warmed and coated with paraffin) forms a well as deep as the tissue which is to be mounted. The block of tissue is then placed in position at the bottom of the well, arranged to cut to the best advantage, and melted paraffin poured in until the well is filled. This is allowed to cool and the paper removed. The paraffin is now gray, appears granular, and is said to be in the crystalline form; if put in a warm place (care being taken that it is not warm enough to melt the paraffin)

FIG. 21.—STENDER DISH.
Useful for dehydrating and preparing tissues for infiltration; also for stains, etc.

it soon becomes transparent, or, it is said, the paraffin becomes amorphous or hyaline.

FIG. 22.—NAPLE'S PARAFFIN BATH FOR INFILTRATING TISSUES IN PARAFFIN.

The apparatus consists essentially of a series of receptacles for holding the melted paraffin, with a surrounding water-bath retained at an even temperature by a thermo-regulator.

The block is now ready to cut. It is trimmed down to near the tissue, each side being cut so as to present a surface

FIG. 23.—FORCEPS, CONVENIENT FOR HANDLING COVER-GLASSES, BLOCKS OF TISSUES, AND SECTIONS.

square to the knife, the general aspect of the block being a

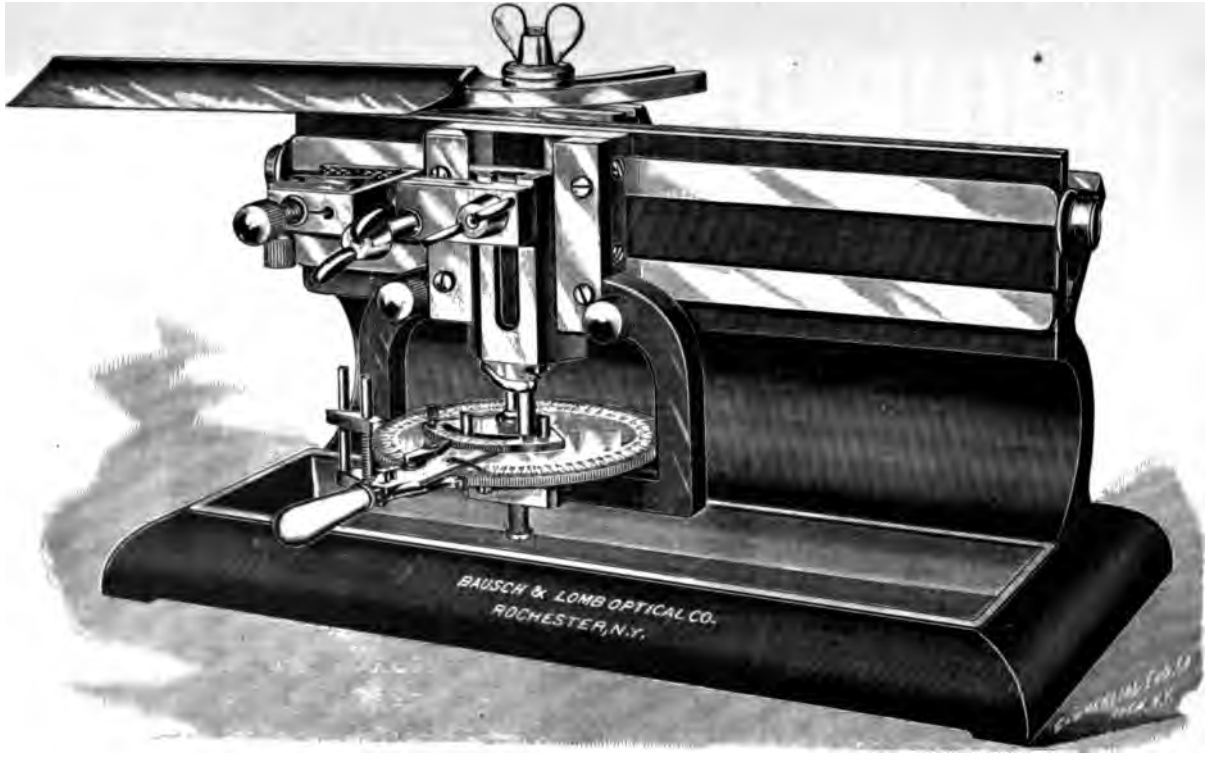

FIG. 24.—LABORATORY MICROTOME.

Can be used, as shown in the cut, for celloidin sections; an attachment for freezing may may be substituted for the clamp shown in the illustration immediately below the knife. For paraffin blocks the knife must be turned with its cutting edge at a right angle to the plane of the knife carrier.

truncated pyramid. The paraffin trimmed off is remelted, and may be used many times. The block is clamped in the holder of the microtome so that the cutting edge of the knife strikes its whole length squarely against the block; the knife is so arranged that it cuts like a chisel, and not with a drawing motion. To get the best sections the paraffin must be of the proper temperature, as this determines the density; in summer the block may have to be cooled by ice, in winter it may require warming.

It will be seen that the above process requires days, and to overcome this objection Reeves has commended the following: (1) Fix in saturated alcoholic solution of corrosive sublimate one hour. In this, fixation and dehydration go on together.

FIG. 25.—SMALL MICROSCOPIC SCISSORS.
Suitable for trimming sections and labels and for other microscopic work.

(2) Absolute alcohol, one hour. (3) Xylol, one hour. As xylol has a very low volatilizing point, it quickly evaporates in the paraffin bath, and permits the rapid penetration of the paraffin, in which it is kept one hour in the first and one hour in the second, when it is cast. In order to prevent the crystallization of the paraffin, the cast is plunged into ice water as soon as its surface has slightly cooled so as to form a thin film, which may be facilitated by holding the block out of the window in winter or gently blowing upon it in summer. The cast is now trimmed and cut. Of course the pieces of tissue to be prepared in this way must be very small, not over 0.5 cm. cube, and the results can not be considered as comparable to the slower method already described.

Mounting Paraffin Sections.—If the sections be properly cut, and the infiltration has been satisfactory, they will adhere in chains or ribbons as they come away, or each section may be removed from the knife as rapidly as cut, using a short sable brush for the purpose. To insure thin sections the knife must be of the utmost sharpness. Before the sections are cut it is best to prepare the slips to receive them. The slips or slides are thoroughly cleansed with alcohol and dried, using a soft

FIG. 26.—RYDER MICROTOME.

Expressly adapted for paraffin sections and cutting in series; can not be used for frozen sections. Can be used for celloidin if the chloroform method of hardening has been adopted.

cloth or toilet paper for that purpose. Place on the center of the slide a very small quantity—less than a drop—of Mayer's albumin, and with a perfectly clean finger wipe it off. This leaves an almost imperceptible layer of the albumin. On this place a few drops of water,—enough to just float the section clear of the albumin,—and place the section on the water; gently warm the slide, being careful not to melt the paraffin; as the section warms it will straighten out, all folds and

wrinkles disappearing. Now carefully pour off the excess of water, and the section falls upon the layer of albumin, to which it adheres. Mayer's albumin is composed of egg-albumen and glycerin, of each 100 c.c., to which 1 gm. of salicylate of sodium has been added to aid the glycerin in preserving the albumin ; after thoroughly mixing, the mass is filtered through paper,—a process requiring weeks. The albumin fixes the section to the slide so that it may be taken through the subsequent processes without the least trouble.

FIG. 27.

Blocks of tissue infiltrated with celloidin or paraffin may be cut in sections free-hand with an ordinary razor; better results may be obtained by even so simple a microtome as the above (Ranvier's microtome), or very much better results by the Ryder or Bausch and Lomb instruments. (*Illustration from Gould's Dictionary.*)

After the section has been drained of the water upon which it was floated to facilitate straightening out, it is placed in a drying oven to get rid of any remaining water. In ordinary work, where no great haste is demanded, the slide may be placed in some warm place, protected from the dust, until perfectly dry. After drying, which may require from four to twenty-four hours, the slide is gently warmed until the paraffin just melts, and no more ; it is then thrust into ordinary kerosene, or, what is slightly better but much more expensive,

xylol; either of these quickly removes the paraffin, usually requiring about fifteen minutes; wipe off the excess of xylol, rinse the slide in alcohol, and place the slide in that liquid until the xylol is removed. From the alcohol the section is stained as will be directed later. If the tissue was fixed in corrosive

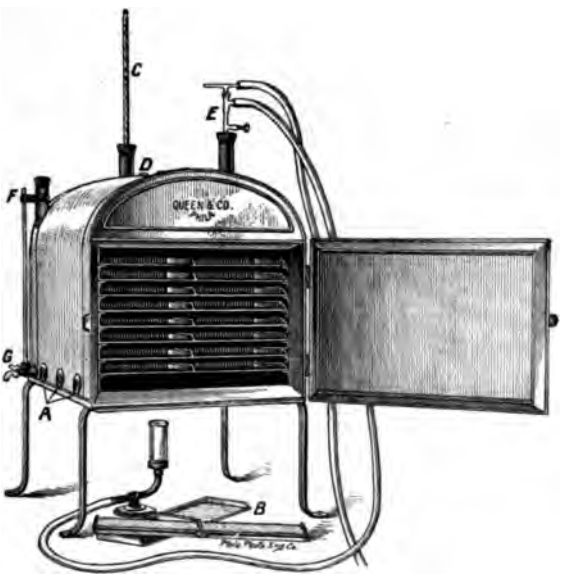

FIG. 28.—DRYING OVEN.

A. Three tubes for admitting air to interior. At *D* are three similar exit tubes. *B*. Shelves upon which slides are placed at the student's desk, from which, after labeling each slide and placing under the slides a piece of paper with his name and desk number, he places the tray in the oven. *C*. Thermometer. *E*. Thermo-regulator. *F*. Water-gage. *G*. Cock for emptying the water space. The temperature of the oven should never reach the melting-point of the paraffin, and had best be between 37° C. and 40° C.

sublimate, this must be removed by treating the section with tincture of iodin, in which it is immersed for fifteen minutes; it is then washed with a few drops of alcohol and placed in a jar of alcohol, from which it is removed for staining when desired.

(2) *Celloidin Infiltration.*—Celloidin is a proprietary product

first used in wet plates for photography, and is nothing more than a non-explosive guncotton. As used, it is dissolved in equal parts of alcohol and ether, thus making a collodion which, so far as I can observe, has no advantage over a good collodion made from guncotton. As ordinarily used, two solutions are needed—one a thick, syrupy solution, and a second thin solution made by diluting the thick solution with an equal quantity of alcohol and ether. The tissue to be infiltrated is fixed and dehydrated as already described for paraffin; it is then placed for twenty-four hours in a mixture of equal parts of alcohol and ether. From this the tissue is transferred to the thin solution of celloidin. The best results are ob-

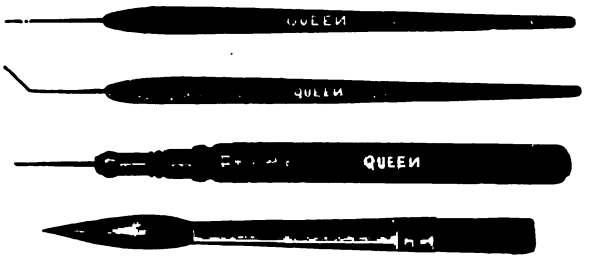

FIG. 29.—NEEDLES AND BRUSH SUITABLE FOR HANDLING SECTIONS.

tained by leaving the mass for infiltration several days in this solution, when it is placed for an equal length of time in the thick solution. A block is then soaked in alcohol and ether for one or two hours or longer, and one end coated with celloidin and wrapped with paper as already directed for paraffin. Into the well the infiltrated piece of tissue is placed, arranged as desired for cutting, and the thick celloidin solution poured over it; the mass, which is now said to be cast, is placed under a lightly fitting bell-jar or cover until the celloidin begins to set, when it is thrown into 80 per cent. alcohol for hardening. At the end of twenty-four hours it will be found sufficiently hard for cutting, but may be kept indefinitely

in the alcohol and cut when desired. Unlike paraffin, celloidin must be cut with the microtome knife at an angle to the block,—that is, with a drawing motion,—and, while the paraffin was cut with a perfectly dry knife, the celloidin must be cut with a knife kept flooded with 80 per cent. alcohol. Each section is removed from the knife as cut and transferred to 80 per cent. alcohol, in which it may be preserved until wanted for use. The great advantage claimed for celloidin is that it does not, like paraffin, have to be dissolved out before the section is stained. Stains such as carmin and hematoxylin may be used, the celloidin holding the sections together during the manipulations incident to staining. A better method of infiltrating is that devised by Gilson, in which, after dehydration and treating with the alcohol and ether mixture, the tissue is placed in a test-tube containing several centimeters of thin celloidin solution ; this is immersed in a water or paraffin bath at about 42° C., at which temperature the solvents (alcohol and ether) rapidly evaporate,

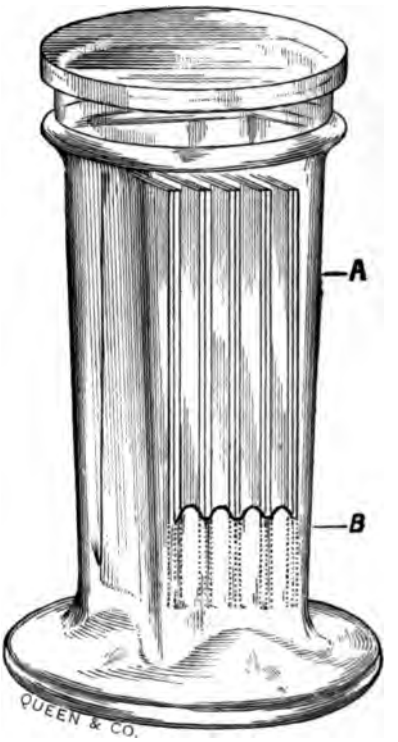

FIG. 30.—DISH FOR REMOVING PARAFFIN, CORROSIVE SUBLIMATE, AND FOR DEHYDRATING.

May also be used for staining, and for the same purposes as the Stender dish. After the sections are cemented on the slide, the slides A are placed back to back and slipped down in the groove B at the bottom of the dish. If the slides are thin, the dish will hold ten at one time.

and thereby hasten penetration. When the solution has evaporated to about one-third its original bulk, it is turned out and cast as in the slow process. The hardening of the block is greatly facilitated, and the results improved, by hardening in chloroform. The process is applicable to blocks which have been infiltrated by the slow as well as the rapid method. As soon as possible after the cast is made the mass is placed in a desiccator or sieve dish, or a bottle with tightly fitting stopper, which has a teaspoonful of chloroform poured on the bottom. A support is arranged above the chloroform on which the block to be hardened is placed, and the vessel tightly closed. Two to twelve hours will be sufficient for the hardening, when it is placed in a mixture of cedar oil two parts and chloroform one part; more cedar oil is added from time to time until nearly pure cedar oil is attained. The sections are cut dry as in the paraffin method. The block may be preserved indefinitely in the cedar oil. After cutting, the sections are washed in alcohol to remove the cedar oil, and may then be stained.

(3) *Congelation Method.*—Fresh tissue may be frozen and sectioned, but the best method is that of Hamilton: (1) Harden. (2) Wash out the hardening fluid. (3) Place in sugar solution two to twenty-four hours. (This solution is composed of two ounces of sugar dissolved in one fluidounce of water.) After removing from the syrup, wash lightly in water and place in (4) mucilage for two hours; the tissue may now be put on the drum of the freezing microtome, frozen, and cut. Remove sections from the knife with a soft brush, and wash thoroughly in water to remove the gum and sugar; the staining is proceeded with as for other sections.

Remarks on the Above Processes.—For small pieces of tissue the paraffin method is best; thinner sections can be cut, and the method of cementing them on the slide makes the handling most convenient. For large blocks, such as an eye, and

for tissues from the brain, spinal cord, or larger nerve trunks, celloidin is to be preferred. After using the freezing method to a very large extent for about ten years, I am thoroughly convinced that it is not to be relied upon. The ice crystals which form in freshly frozen tissue break up the cells and give results which may mislead the most experienced investigator. The distortion of structure incident to the use of congelation masses, their macerating properties, and the difficulty in removing the infiltrate, have led me to give them up entirely for laboratory work; only the crudest kind of pathologic work can be done by the method, and the results are always open to criticism.

Staining and Mounting.—The two stains most used in laboratory work are carmin and hematoxylin. Strongly alkaline stains such as lithium-carmin are no longer to be commended; the same is true of bulk staining. The *carmin* most useful in the laboratory is Grenacher's alcoholic borax-carmin:

Alcoholic Borax-carmin.

Carmin (best No. 40), ... 3 parts.
Borax, ... 4 parts.

Mix and pulverize thoroughly in a mortar and add 100 parts of water; boil for one-half of an hour; add an equal bulk of 70 per cent. alcohol; set aside for one week, and then filter.

To stain, add enough of the stain to the section on the slide to abundantly cover it, and allow it to act from five to ten minutes or longer. Drain off the excess of stain, wipe around the section with paper or soft cloth, and apply acid alcohol.

Acid Alcohol.

Hydrochloric acid, ... 1 part.
Water, ... 29 parts.
Alcohol, ... 70 parts.

The section, as soon as the acid alcohol is applied, turns from a purplish-red to a light crimson, and becomes more

nearly transparent; it is then washed in strong alcohol, the excess wiped from around the section, and the latter covered with creosote. The alcohol dehydrates and removes the acid, which is the differentiating agent, and the creosote renders the section clear for examination by transmitted light. As soon as the section is clear, remove the excess of creosote, apply a drop of balsam, and cover with a thoroughly cleansed cover-glass; label the section. It will now keep indefinitely.

FIG. 31.—DROPPING BOTTLE, WITH BARNES' DROPPER, WHICH CLOSES THE MOUTH OF THE BOTTLE LIKE A RUBBER STOPPER.

These bottles are usually of one ounce capacity, and are convenient for holding stains and staining reagents.

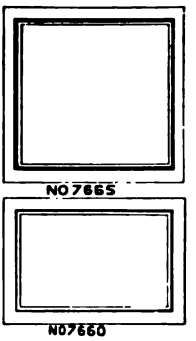

FIG. 32.—PROPER SIZE LABELS FOR LABELING MICROSCOPIC SLIDES.

Hematoxylin Staining.—One of the best forms of this stain is Delafield's, made as follows: Dissolve 4 gm. of hematoxylin crystals in 25 c.c. of strong alcohol; add this solution to 400 c.c. of a cold, filtered, saturated aqueous solution of ammonia alum; expose to light and air for several days. Filter and add:

Glycerin, ...	100 c.c.
Methylic alcohol, ...	100 c.c.

Allowed to stand in the light, with the bottle loosely corked; this turns dark purple, almost black, when it should be filtered

and kept in tightly stoppered bottles. For use it should be much diluted ; the amount of dilution must be determined for each lot, varying with the degree of oxidation and the age of the stain. If made with distilled water, and all vessels and containers kept chemically clean, this stain will keep for years. To use it, the sections on the slide, prepared as already directed, are covered with the diluted stain for from five to fifteen minutes, washed with water, dehydrated in alcohol, cleared with creosote, and mounted in balsam as directed in the last steps for carmin, except that differentiation is secured by the use of water and not acid alcohol. A better stain is secured by taking enough distilled water in a bottle or staining dish to immerse the slide on end ; to this add enough of the hematoxylin to just a little more than color the water ; the sections cemented on the slide are left in this all night (or even twenty-four hours), washed in water, and treated as above. Hematoxylin not only stains the nucleus, but affords a light tint to the protoplasm as well. This latter, however, can be better secured by using eosin. After the section is stained in hematoxylin and washed in water, the excess of the water is removed and the section treated for a moment in an alcoholic solution of eosin, followed by alcohol and creosote, and mounted in balsam. The nuclei are stained purple by the hematoxylin and the cell protoplasm pinkish by the eosin. It makes a very fair contrast stain, and brings out some pathologic bodies not shown by the hematoxylin. In addition, it shows red blood-corpuscles to the very best advantage, being a specific stain for hemoglobin.

QUESTIONS.

(1) How make sections of fresh tissue? (2) What is meant by "killing" and "fixing" tissues? (3) What is Flemming's solution? (4) What is Hermann's solution? (5) How is corrosive sublimate used for "fixing" tissues? (6) What agents are used for hardening nerve tissues?

(7) What is Müller's fluid? (8) What is Erlicki's solution? (9) Give the steps of dehydration and describe infiltration by the paraffin method. (10) How mount the tissue on a block? (11) Give the steps in Reeves' rapid method of fixation and paraffin infiltration. (12) Describe method of cutting sections of tissue infiltrated by the paraffin method. (13) What is Mayer's albumin? (14) How cement section to slide? (15) How remove paraffin from sections? (16) If tissue has been hardened in corrosive sublimate, how must the sections be treated? (17) Give the steps for infiltration by celloidin. (18) Describe Gilson's rapid method for infiltrating with celloidin. (19) Describe the congelation method. (20) What is borax-carmin? and describe its method of use. (21) Give technic of logwood stain.

CHAPTER III.

MICROSCOPIC EXAMINATION OF URINE.

A Desirable Laboratory Microscope.—Figure 33 illustrates a stand useful in a pathologic laboratory. The horseshoe base gives solidity by its long arms and great weight.

FIG. 33.

To this base is attached the upright which supports the superstructure; the stand should be handled by this piece entirely, never grasping the parts above in moving the micro-

scope, as such a procedure is likely to injure the adjustments. At the upper termination of the upright is the joint for inclining the microscope for convenience in working. Running to the front from this joint is the stage upon which the slide is placed for examination ; clips are shown for retaining the slide in position. Beneath the stage are the sub-stage mountings, consisting of diaphragms for lessening the light, condensers for increasing the rays' intensity, and a mirror for reflecting the light upward through the optic axis of the instrument. These parts are adjustable by lateral movement, by rack, pinion, and screw motion. Behind the inclination joint what is known as the upright arm rises; at its upper part is placed the fine adjustment, worked by a milled thumbscrew. Passing off in front of this upright arm is the horizontal arm to which is attached the coarse adjustment by rack and pinion moved by the milled heads shown at both sides. The tube carrying the optic parts is attached to the horizontal arm by the rack and pinion coarse adjustment. The tube is so made that it may be drawn out to a standard length. At the upper end of the tube is the eyepiece, at the lower end the objective. In the laboratory instrument two objectives ($\frac{2}{3}$ of an inch and $\frac{1}{6}$ of an inch) are mounted on a double nosepiece, by means of which either objective may be brought into use. In nearly all cases the examination should *begin* with the lower power, followed *if necessary* by the higher power.

To Use the Microscope.—The instrument is placed in front and slightly to one side, usually the right side, of the observer, and tilted at the joint so as to afford a comfortable position for observation without craning the neck or stooping the shoulders. By daylight, northern light, or light from white clouds, or if the window is exposed to the direct rays of the sun, a piece of thin tissue-paper is pasted over the glass, or the glass may be frosted or painted; direct sunlight should never be used except for photomicrography. If an artificial light is to be

used, the microscope is placed about 30 cm. from the light, and to one side, so that neither the heat nor the direct rays from the light will be thrown in the face or eyes of the observer. While for convenience in general work the stand is tilted, when examining mounts of liquids, urine, hanging-drop culture, etc., the stand must be upright so that the stage is perfectly level. Place the slide on the stage and loosely secure it by the clips; so adjust the mirror as to illuminate the center of the field; without placing the eye to the eyepiece, rack the objective down until it almost touches the slide; then look into the instrument and perfect the illumination by adjusting the mirror again, if necessary; slowly focus *upward* by the coarse adjustment until a satisfactory focus is obtained; in moving the slide about the fine adjustment will be all that will be necessary. *Never* focus downward until you have mastered the method just given; careless, or even at times the most careful, downward focusing will crush the slide or the lens by passing over the true focus and jabbing the objective into the slide. Before removing the slide, always rack the objective upward until it is at least ½ of an inch from the slide.

Method of Conducting the Examination.—The urine should be collected in a conical glass, and protected from dust and allowed to stand for twenty-four hours. When the deposit has settled, a pipet, closed by the finger at the upper end, is introduced and some of the deposit allowed to enter. The fluid on the outside of the pipet is then removed with a cloth, and, holding the pipet perpendicularly, a small drop is placed on the slide and a cover-glass applied. Drain off excess of fluid with blotting-paper, and examine with ⅔ of an inch and ⅙ of an inch objectives. The sediment can be examined with more satisfaction by adding one drop of Gram's solution to the fluid placed on the slide for examination. For *formula* of Gram's solution see section on "Bacteriology."

Preservation of the urine may be aided by adding a crystal of thymol, camphor, or menthol, or a few drops of tincture of iodin or Gram's fluid. If it be desired to preserve the sediment, this is best accomplished by carefully decanting the supernatant fluid and adding an equal quantity of a saturated aqueous solution of potassium acetate, allowing this to remain forty-eight hours, again decanting, and adding fresh acetate solution. After

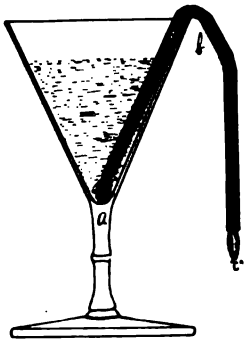

FIG. 34.—CONIC GLASS SUITABLE FOR THE SEDIMENTATION OF URINE.—(*Coplin and Bevan.*)

In position is shown a candle-wick filter for securing urinary sediment. The filter consists of a glass tube so bent that the longer arm is outside and opens below the level of the bottom of the conic glass. Through the bent glass tube is drawn a few strands of candle-wick to fill the tube rather tightly. By capillarity the urine rises in the bent tube and eventually flows over; in so doing it deposits all the sediment on that end of the candle-wick which is at the bottom of the glass. This is gently brushed over a number of slides, cover-glasses applied, and the slides examined at once.

FIG. 35.—CENTRIFUGE WITH HEMATOCRIT ATTACHMENT.

The attachment for sedimenting liquids such as urine is shown attached. This may be lifted off and the hematocrit attachment shown in the upper part of the figure substituted in the place of sedimenting attachment shown in position. There are two gears, one for sedimenting blood, known as the high gear, and which gives 10,000 to 14,000 revolutions a minute; the lower gear, for sedimenting urine, gives from 2500 to 4000 revolutions a minute. The crank is easily transferred from one gear to the other.

repeating this three times, no difficulty will be found in preserving casts, blood, epithelium, etc., present in the sediment.

The **centrifuge** can be used to great advantage in the sedimentation of urine. Two specially constructed test-tubes filled with urine, surrounded by aluminium cylinders, are made to revolve with a speed of 4000 revolutions per minute. Sediment can be obtained from fresh urine in a few minutes by this method, and where large numbers of specimens are examined each day this instrument is invaluable.

ORGANIZED SEDIMENT (*Cellular Constituents*).—*Red Blood-corpuscles.*—When these corpuscles occur in large numbers and in good condition without being intimately blended with the urine, they are usually from the bladder or urethra; but when they do not form a red sediment after many hours' standing, and have lost their coloring matter and appear as pale-yellow, washed-out rings (phantom corpuscles of Traube), especially if associated with blood-casts, the hemorrhage has probably occurred in the substance of the kidney, renal pelvis, or ureters.

Pus.—Urine containing pus in any quantity is always turbid when voided, and shows decided reaction for albumin if the quantity of pus be at all large. Pus-corpuscles are nearly twice the size of red blood-corpuscles, and appear as pale, circular, granular discs with several nuclei, and are practically identical with mucous corpuscles, white blood-corpuscles, and lymph-cells.

They may show ameboid movements when examined in the fresh state, but, as seen in urinary sediment, their protoplasm is coagulated into coarse granules.

Epithelium.—(Make drawings of different forms.)

Squamous epithelium.

Transition epithelium.

Epithelium from bladder.

Urinary Casts.

I. Those consisting of cells.

II. Those which consist of the products of cellular change.

III. Hyaline casts.

Examine with $\frac{1}{6}$-inch objective and make drawings.

Blood casts.

Epithelial casts.

Granular casts.

Waxy casts.

Fatty casts.

Hyaline casts.

Pus casts.

Bacterial casts.

Cylindroids.

False casts, composed of urates or crystals.

Casts from seminal tubes.

Spermatozoa are thread-like bodies, 50μ long, provided with a head and a long, tapering, tail-like extremity.

Their constant deposit indicates spermatorrhea. Stain; place dry cover-glass specimens in carbolfuchsin for two seconds, and wash in water; *dry*, mount in balsam.

Non-pathogenic Fungi:

Molds, or large segmented rods.

Yeast plants (saccharomyces urinæ) are arranged in bead-like forms with budding cells attached.

Bacteria of decomposition.

Pathogenic Fungi.—*Tubercle Bacilli.*—In all cases of purulent urine, accompanied by anemia, wasting, and evening temperature, the urinary sediment should be examined for tubercle bacilli.

Purulent deposits of tuberculous urine should be treated the same as sputum in searching for tubercle bacilli. The centrifuge aids materially in this examination. Experience shows

that residual urine drawn with a catheter after the patient has apparently voided all the contents of the bladder, is more likely to contain tubercle bacilli than the tidal urine.*

Gonococcus (Neisser). — Minute, roll-shaped diplococcus found in urine containing gonorrheal pus. (For method of staining and description see article on "Bacteriology.")

Distoma Hematobium.—The eggs of this parasite, about 125μ in length, are oval or flask-shaped, and are found accompanied by blood-cells and pus.

Filaria Sanguinis Hominis.—The embryos are occasionally found in chyluria. (See "Animal Parasites.")

UNORGANIZED SEDIMENT (*Crystalline and Amorphous*).

Sediment of Acid Urine.—(Examine and draw the various crystals.)

Uric acid (whetstone crystals).
Oxalate of lime (envelope crystals).
Hippuric acid.
Urate of soda.
Tyrosin and leucin.
Soaps of lime and magnesium.
Amorphous deposits.
Urates.
Brown and yellow concretions.

Sediment from Alkaline Urine.

Triple phosphates (coffin-lid crystals).
Urates of Ammonium (hedgehog crystals).
Indigo.
Cholesterin.
Amorphous deposits.
Phosphate of lime.
Carbonate of lime.

* Byrson, American Association of Genito-urinary Surgeons, May 6, 1897.

ILLUSTRATIONS OF VARIOUS URINARY SEDIMENTS.*

FIG. 36.—PHANTOM AND DISTORTED RED BLOOD-CELLS FOUND IN URINE, MOST COMMONLY THAT OF RENAL HEMATURIA. —(*Landois.*)

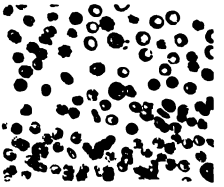

FIG. 37.—BLOOD-CELLS IN THE URINE.—(*Gould.*)

The cells which appear almost normal could not have been subjected to the action of the urine but for a short time.

FIG. 38.—BLOOD-CELLS IN THE URINE, LYMPH-CORPUSCLES (LEUKOCYTES OR PUS-CELLS), AND CRYSTALS OF TRIPLE-PHOSPHATE.—(*Landois.*) × 350 diameters.

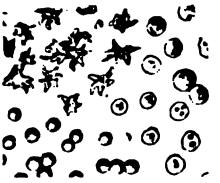

FIG. 39.—PUS-CELLS IN URINE.—(*Gould.*) Many are irregular or fragment forms.

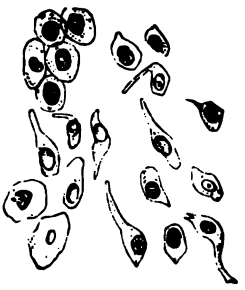

FIG. 40.—EPITHELIUM FROM THE CONDUCTING PART OF THE URINARY APPARATUS, MOSTLY FROM THE BLADDER.

Note in the upper left part of the figure the cells which resemble renal epithelium.

FIG. 41.—RENAL EPITHELIUM.

The four cells below and to the left are fatty. This form of epithelium will be found on casts and free in the urine. It will be noted, however, that it so closely resembles epithelium from one layer of the conducting apparatus that the diagnosis of free renal epithelium may be open to criticism. See figure 40, epithelium from the bladder.

* Experience has convinced the writer that the best way to learn to recognize the various urinary sediments is to take as good an illustration, or series of illustrations, as can be secured, and work at the microscope with the illustrations at hand until able to recognize all the ordinary forms.

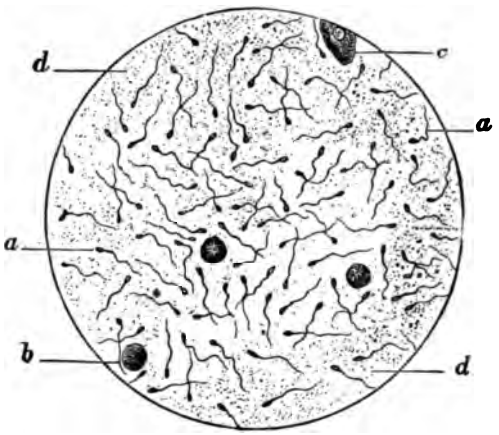

FIG. 42.—SEMINAL ELEMENTS, SOME OF WHICH MAY BE FOUND IN URINE.
a. Spermatozoa. *b*. Seminal cells. *c*. Epithelium. *d*. Seminal granules.

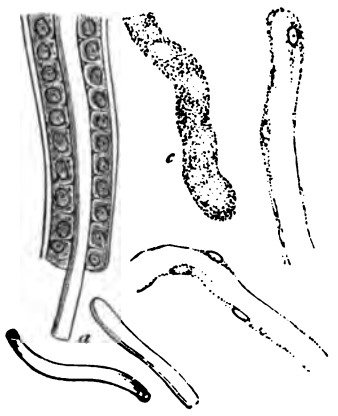

FIG. 43.—ILLUSTRATING THE FORMATION OF CASTS.—(*Rindfleisch.*)
a. Hyaline cast in place. If it comes away bringing nothing with it, it will remain a hyaline cast. If it brings epithelium, it will be an epithelial cast; if the epithelium is granular, it will be a granular cast; if fatty, a fatty cast. *c*. Granular cast.

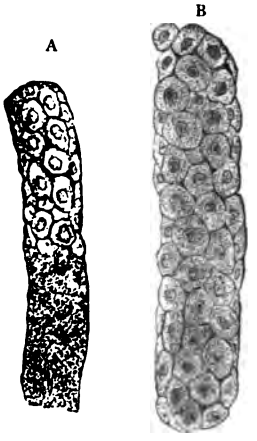

FIG. 44.—EPITHELIAL CASTS.—(*Landois.*)
A. Epithelial cast, the lower end of which is coarsely granular. B. Epithelial cast in which the epithelial cells, though themselves granular, have not broken up.

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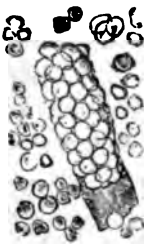


FIG. 45.—BLOOD-CELLS AND BLOOD-CAST.—(*Landois.*)

FIG. 46.

A. Hyaline cast. B. Hyaline cast with a few attached leukocytes. C. Hyaline cast with attached epithelium, truly an epithelial cast.—(*Landois.*)

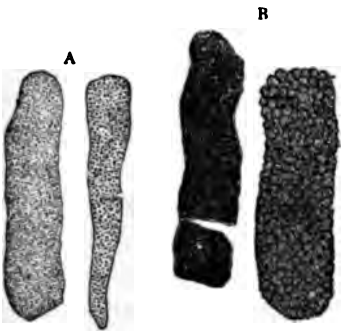


FIG. 47.—GRANULAR CASTS.—(*Landois.*)

A. Granular casts, in which the granules are fine and the dissolution of the epithelial cells complete. B. Granular casts, in which the granules are coarse and the outlines of the epithelial cells at points faintly distinguishable.

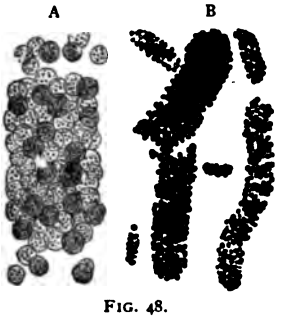


FIG. 48.

A. Cast made up almost purely of leukocytes. B. Casts composed of acid sodic urate; a crystalline cast.—(*Landois.*)

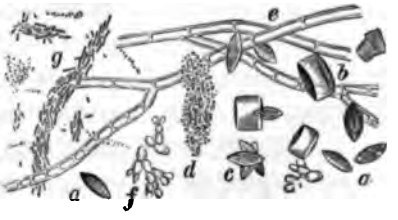


FIG. 49.

a, *b*, *c*. Crystals of uric acid. *d*, *g*. Zooglea masses of bacilli and cocci. *e*. Mold. *f*. Yeast.—(*Landois.*)

FIG. 50.—SOME FORMS OF URIC ACID.

1. Rhombic crystals. 2. Whetstone forms. 3. Quadrate forms. 4, 5. Irregular forms. 6, 8. Groupings into rosette forms. 7, 9. Bundle forms, precipitated by adding hydrochloric acid to the urine. The crystals may be pigmented or lightly colored brownish-yellow; the pigment is presumed to be uroerythrin, also called urochrome.—(*Landois.*)

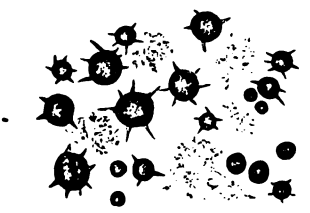


FIG. 51.—ACID AMMONIUM URATE.

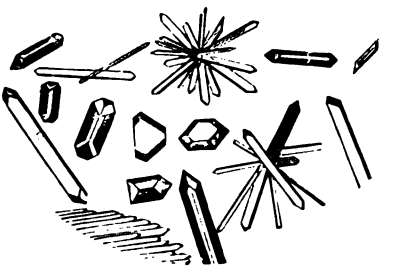


FIG. 52.—HIPPURIC ACID. FOUR-SIDED PRISMS WITH TWO OR FOUR BEVELED EDGES.—(*Gould.*)

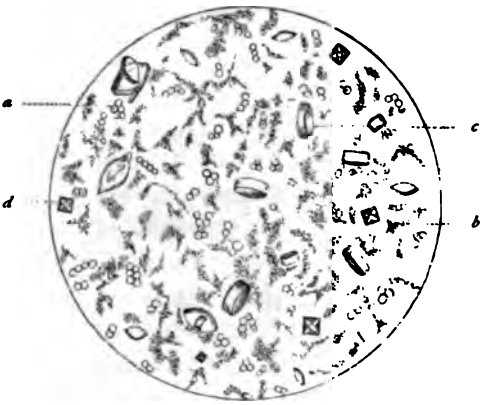


FIG. 53.—SOME DEPOSITS IN ACID FERMENTATION OF THE URINE.—(*Landois.*)
a. Bacteria. *b*. Amorphous sodic urate. *c*. Uric acid. *d*. Calcium oxalate.

FIG. 54.—SOME DEPOSITS FROM AMMONIACAL URINE. (ALKALINE FERMENTATION.)
a. Acid ammonium urate. *b*. Ammoniomagnesium phosphate. *c*. Bacteria.

FIG. 55.—WHETSTONE AND IRREGULAR CRYSTALS OF URIC ACID.—(*Gould.*)

FIG. 56.—AMMONIUM URATE. "HEDGEHOG" CRYSTALS.—(*Gould.*)

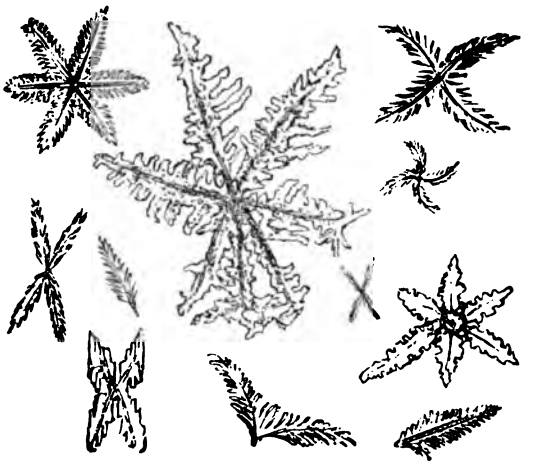


FIG. 57.—STELLATE AND FEATHERY CRYSTALS OF TRIPLE PHOSPHATE.—(*Tyson.*)

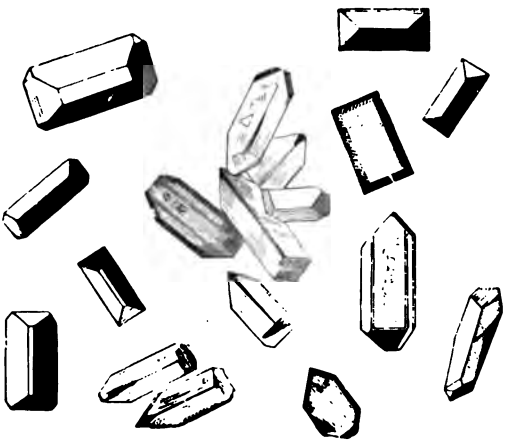


FIG. 58.—FORMS OF CRYSTALS OF THE AMMONIOMAGNESIUM PHOSPHATE.—(*Tyson.*)

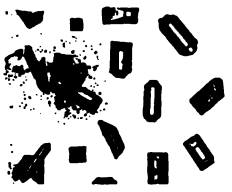


FIG. 59. — AMMONIOMAGNESIUM PHOSPHATE (TRIPLE PHOSPHATE).—(*Gould.*)
Triangular prisms with beveled edges; "coffin-lid" crystals.

FIG. 60.—MAGNESIUM PHOSPHATE.—(*Gould.*)
Elongated rhombic tablets, which may be fused together in variously formed masses.

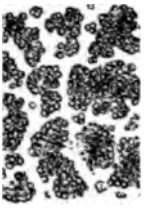


FIG. 61.—AMORPHOUS GRANULES OF CALCIUM CARBONATE.—(*Gould.*)

FIG. 62.—OXALATE OF LIME.

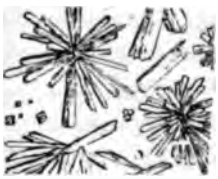


FIG. 63.—AMORPHOUS GRANULES, WEDGE-SHAPED CRYSTALS, SOME ARRANGED IN ROSETTES, OF CALCIUM PHOSPHATE.—(*Gould.*)

FIG. 64.—DUMB-BELL AND OCTAHEDRAL CRYSTALS OF CALCIUM OXALATE.—(*Gould.*)

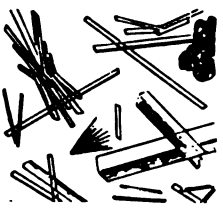


FIG. 65.—CALCIUM SULPHATE; ELONGATED TRANSPARENT NEEDLES OR TABLETS.—(*Gould.*)

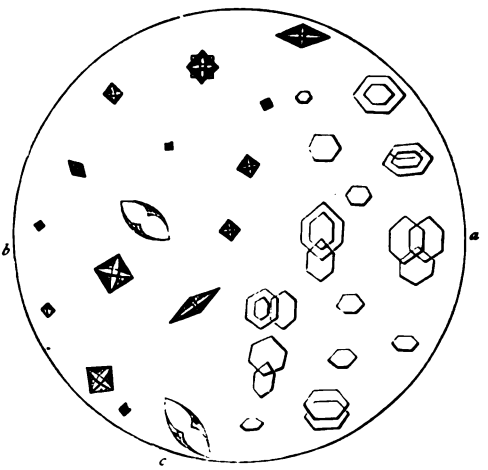


FIG. 66.

a. Crystals of cystin. *b*. Crystals of oxalate of lime. *c*. Hour-glass forms of *b*.

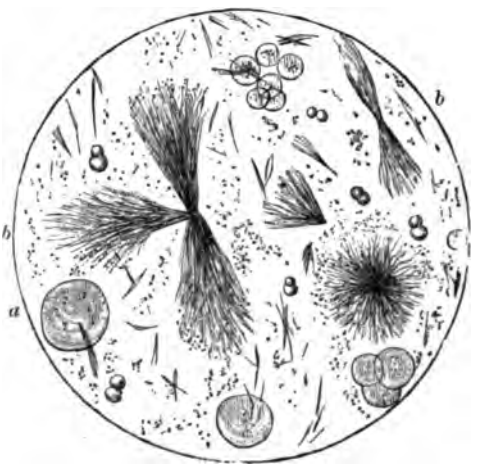


FIG. 67.

a. Leucin balls. *b*, *b*. Tyrosin sheaves.

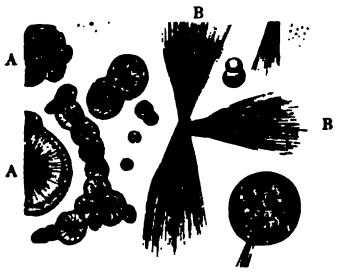


FIG. 68.—LEUCIN AND TYROSIN.

A, A. Leucin; yellowish, highly refracting spheres with radiating lines. B, B. Tyrosin, needles and sheaf.

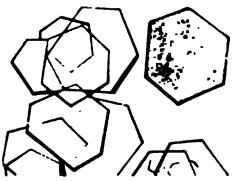


FIG. 69. — CYSTIN, SIX-SIDED PLATES OFTEN SUPERIMPOSED.—(*Gould.*)

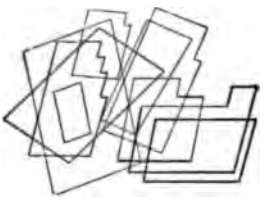


FIG. 70.—CHOLESTERIN.—(*Landois.*)

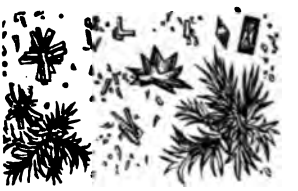


FIG. 71.—INDIGO.—(*Gould.*)
Amorphous granules, fine needles, and crystals of a blue color.

QUESTIONS.

(1) Describe a microscope. (2) What is the proper position in which to place a microscope, and how secure the best illumination? (3) Give methods for sedimenting urine and what agents may be used for its preservation. (4) Describe the microscopic appearances of the organized sediments which may be found in urine. (5) What varieties of epithelium are found in urine? (6) Name different forms of casts. (7) Give a description of each form and the method by which casts originate. (8) What bacteria occur in urine? (9) What crystalline and amorphous precipitates may be found in (*a*) acid urine, (*b*) alkaline urine? (10) Make drawings of each element likely to be found in urine. (Note: With but little effort, combined with considerable practice, the student can make drawings of any of the ordinary sediments, and he should be able to do so.)

CHAPTER IV.

TECHNIC OF SPUTUM EXAMINATION.

Collecting the Specimen.—Great care should be exercised in obtaining the sputum for examination. Have the patient expectorate directly into a small stone cup or sterilized salt-mouth bottle, which should be at once sealed with adhesive plaster or tightly corked, and labeled. When ready for examination, the sputum should be poured upon a piece of ordinary window glass with one side painted black, or a Petri dish placed over a blackened surface. From this black surface the small, white, opaque portions, which are best for examination, can be readily seen, removed by forceps or platinum hook, and placed in the center of a glass slide. A cover-glass is laid on the specimen, and slight pressure made to obtain a uniform layer.

FIG. 72.—SQUAMOUS EPITHELIUM.

Often found in sputum and in urine. In the former it is from the mouth or pharynx. In urine it is usually from the vagina.

White blood-corpuscles are found in all sputum.

Red Blood-corpuscles.—Their presence in small numbers is not significant. In pneumonia they occur as pale discoid bodies, and in hemoptysis the sputum may consist almost entirely of red corpuscles.

Epithelium.—Squamous, from the mouth.

Ciliated, usually from the trachea and bronchi.

Alveolar, from the alveoli of the lungs.

Elastic Fibers.—When these fibers display an alveolar arrangement, they have been derived from the pulmonary alveoli, and indicate a destruction of lung tissue.

They occur in tuberculosis and bronchiectasis, and occasionally in pulmonary abscess and pneumonia. The slide of

sputum is prepared in the usual way, and examined with $\frac{1}{6}$ of an inch objective.

The elastic fibers exhibit a double contour, are dark colored, slightly curved, and vary much in length and breadth. They

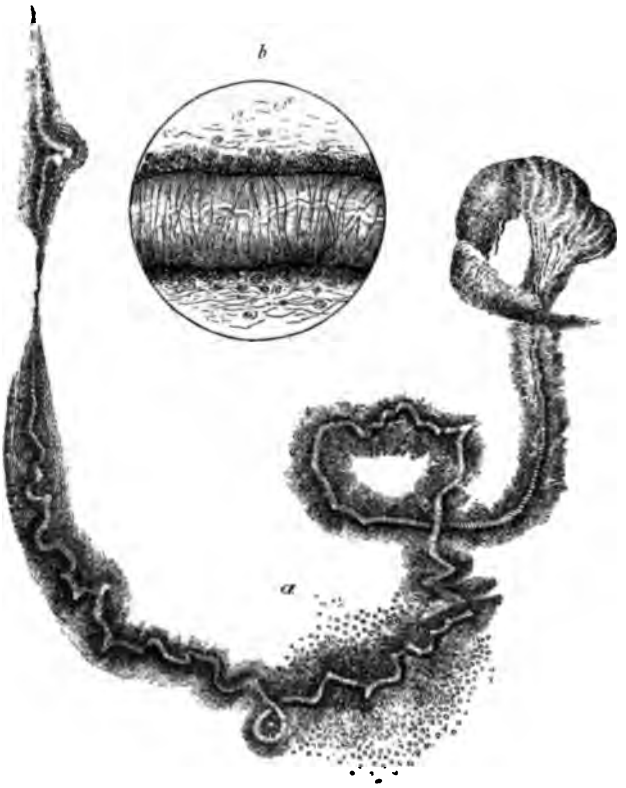


FIG. 73.—CURSCHMANN'S SPIRALS.
a. × 80 diameters. *b*. × 300 diameters.

can be most readily collected for demonstration by rapid sedimentation in a centrifuge.

Curschmann's spirals are found in sputum of asthmatic patients, and appear as thick white bodies having a twisted tubular form. When examined with a low power they show

a central, highly refracting, twisting thread, around which is a meshwork of delicate fibers. They need no stain.

Fibrinous casts are tree-like casts of the terminal bronchial tubes found in bronchitis and pneumonia, and composed of fibrin containing entangled cellular elements (see fibrinous inflammations of mucous membranes).

Charcot-Leyden Crystals.—These crystals are colorless, have a pointed octahedral form, and are found chiefly in the semi-solid, grayish-yellow pellets discharged during an asthmatic attack.

Tubercle Bacillus.—(For technic of examination see article on "Bacteriology.")

FIG. 74.—CHARCOT-LEYDEN CRYSTALS.—(*Landois.*)

Bacillus of leprosy occasionally occurs in sputum. (For technic of examination see article on "Bacteriology.")

Pneumobacillus, Pneumococcus (Friedländer, Fraenkel).—(For technic of demonstration see article on "Bacteriology.")

QUESTIONS.

(1) How obtain sputum for examination? (2) How mount sputum? (3) What are Curschmann's spirals? (4) What is the significance of elastic fibers in the sputum? (5) What are fibrinous casts in the sputum? (6) Describe the Charcot-Leyden crystals? (7) What bacteria are found in the sputum?

CHAPTER V.

TECHNIC OF BLOOD EXAMINATION.

Examination of the Blood.*—Blood is examined microscopically to determine the number and character of the corpuscles, their relative proportion, and the presence of microorganisms and parasites. The estimation of the hemoglobin is also of the greatest importance.

Blood should always be examined in the fresh, unstained condition, and this followed by a study of stained specimens. To obtain the blood, cleanse carefully the lower part of the lobe of the ear, using, first, soap and water, followed by water,

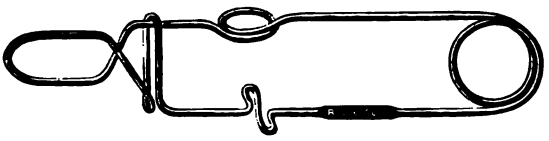


FIG. 75.—STEWART'S COVER-GLASS FORCEP.
Convenient for blood work, and absolutely necessary for bacteriologic work; useful also in sputum work.

alcohol, and ether in the order given, rubbing the ear vigorously to induce hyperemia. With a lance-shaped needle prick the skin quickly and to a good depth; let the first few drops escape and wipe them off, using for examination only the blood which follows. Have at hand at least a dozen cover-glasses carefully cleaned in acid alcohol followed by alcohol and careful wiping; four slides cleaned in the same way should be at hand. A square cover-glass, gently warmed,

* For detailed study of the blood see "Clinical Examination of the Blood," by Richard C. Cabot, M.D.

not hot, is allowed to touch the drop of blood; a droplet adheres, and the cover-glass is inverted, drop downward, on a warm, clean slide. As soon as the blood runs to the edge of the cover-glass, with a sable brush cedar oil is painted around the edge, to exclude air and prevent drying. The slide is now ready for examination. A second and third slide are prepared in the same way. These will not keep, and must be examined at once, using first low powers and then higher. While the blood is flowing another cover-glass is touched to the drop, so that the center of the glass receives the droplet; immediately, a second cover-glass is dropped on the first, care being taken that the corners do not coincide; if the glasses are clean, the blood quickly flows to the edge; at once separate them by sliding

FIG. 76.—FRESHLY DRAWN LEUKEMIC BLOOD.—(*Landois.*)

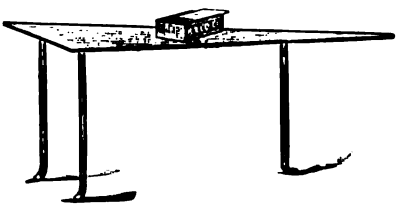


FIG. 77.

Flatiron-shaped copper table which may be used for fixing blood or for paraffin infiltration. If a Bunsen burner be placed under the tip of the sharpest corner, beyond the single leg, and the strip heated to a constant temperature, so that the extreme end from the burner may be cold, any degree of temperature between the cooler part and that over the burner, which is practically red-hot, may be obtained. As shown in the cut, a small paraffin dish is placed over a spot where the paraffin is kept barely melted.

them apart, carefully avoiding any lifting motion; dry quickly, but avoid heating while moist. At least eight or ten spreads should be prepared in this way from each case. These must now be fixed. The best method for fixing is by heat, as in a hot-air

oven or sterilizer at 115° C. for about twenty minutes. In the absence of an oven a copper plate or strip is convenient; a strip five to ten cm. wide and 20 to 30 cm. long, supported over a flame and protected from draughts of air, answers very well. The flame being at one end soon heats the strip so that at any point a fairly constant temperature is maintained; by dropping water on this plate at various points a place is found where water boils; drop the cover-glass on this point, turning the film side down; about twenty minutes will be needed for fixing. Cover-glass films may be fixed by immersion in a mixture of equal parts of alcohol and ether for two hours, followed by drying. After fixation by any of the above methods, the covers may be stained at leisure.

Staining.—The powder for making the Ehrlich-Biondi-Heidenhain stain can be used; the powder is prepared by Grübler; I have tried other makes without success. To prepare the stain use:

Ehrlich-Biondi powder,	1 gm.
Absolute alcohol,	1 c.c.
Distilled water,	6 c.c.

Mix thoroughly and stand aside for at least a week, when an abundant precipitate forms; avoid disturbing this, and use only the supernatant fluid.

If it is desired to make up the stain from its various ingredients, the following stock solutions must be prepared; these are all to be saturated, and the quantities given will insure saturation from most samples, but, as the dyes vary in solubility, different samples may require slightly more or less. As it is best not to filter, and as only the supernatant fluid is to be used, it will be found convenient to make up all of these stains in tall narrow bottles, and, while more expensive, Grübler's stains had best be used.

(1) Saturated aqueous solution of orange G.:

Orange G.,	6 gm.
Distilled water,	100 c.c.

(2) Saturated aqueous solution of acid fuchsin :

Acid fuchsin (Fuchsin S., Grübler), ... 9 gm.
Distilled water, ... 100 c.c.

(3) Saturated aqueous solution of methyl-green :

Methyl-green, OO cryst., ... 6 gm.
Distilled water, ... 100 c.c.

These stock solutions keep well. The mixed stain, prepared from them, has not such good keeping qualities, and, while not ripe for the best results under one week, after two or three weeks usually does not stain so well ; occasionally, however, a sample may give fairly good results for months. A little experience enables one to see which of the three stains is deficient, and by adding a trace of the required stain improve the mixture. Almost no two blood cases stain alike, and, for the best results, slight changes in the formula may be made to overcome this defect. Ehrlich's latest formula, as given by Cabot, and the Johns Hopkins formula, as given by Simon, are as follows, made from the above stock solutions :

	Ehrlich's Formula.	*Johns Hopkins' Formula.*
No. 1, ...	120 to 125 c.c.	18 c.c.
" 2, ...	80 " 165 c.c.	9 c.c.
" 3, ...	125 c.c.	20 c.c.
Glycerin, ...	100 c.c.	5 c.c.
Absolute alcohol, . . .	200 c.c. (94 per cent.)	15 c.c.
Distilled water, . . .	300 c.c.	30 c.c.

Stain the fixed films from two to five minutes, wash in distilled water, dry, and mount in balsam.

To stain the basophilic " mast cell " use :

Saturated alcoholic solution of dahlia, filtered, . . . 50 parts.
Glacial acetic acid, ... 10 to 15 parts.
Distilled water, ... 100 parts.

Stain twenty-four hours, wash in water, dry, and mount in balsam.

To stain malarial parasite: Fix for three or four minutes in absolute alcohol, stain five minutes in Plehn's stain, wash in water, dry, and mount in balsam.

The formula for this stain is:

Saturated aqueous solution of methylene-blue, ... 60 c.c.
One half of one per cent. solution of eosin in 75 per cent. alcohol, ... 20 c.c.
Distilled water, ... 40 c.c.
Twenty per cent. aqueous solution of sodium hydroxid, 12 gtt.

The organisms are easily detected in fresh blood prepared as above; indeed, Laveran advises not to stain.

Forms of Blood-cells.—*Red corpuscles*, or *erythrocytes*, when normal, are biconcave circular discs of a pale yellow color, and are 7.5μ in diameter and 1.5μ in thickness.

Microcytes are small red blood-cells, 2μ to 3μ in diameter,

FIG. 78.—POIKILOCYTES.

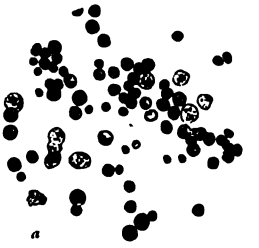


FIG. 79.—TYPES OF RED BLOOD-CELLS; ALSO LEUKOCYTES, AS AT *a*.—(*Landois.*)

which do not run in roulcaux, but are frequently quite numerous, especially in pronounced anemia and toxemias.

Megalocytes are red corpuscles 8μ to 15μ in diameter, much larger than normal, and frequently ovoid.

Poikilocytes are red corpuscles, exhibiting a remarkable variety of shapes; usually found in pernicious anemia.

Normoblasts are deeply stained, nucleated, red corpuscles of ordinary size. The nucleus is about one-half the diameter of the cell, and is usually eccentrically placed.

Megaloblasts, or *gigantoblasts*, are large red cells, about 15μ in diameter, with nucleus occupying most of the cell and staining faintly. The perinuclear structure shows polychromatophilia,—a reaction in which the red cells take up other of the colors in Ehrlich's stain than the orange G; it is believed to be a degeneration phenomenon.

Microblasts are extremely small, nucleated, red forms.

White Blood-corpuscles, or *Leukocytes*.—Ehrlich recognizes the following varieties of white blood-cells:

(1) *Small Lymphocytes*.—Small cells, about the size of a red blood-corpuscle, probably derived from the lymphatic glands. They have a single, large, round, deeply staining nucleus, surrounded by a narrow rim of non-granular protoplasm.

FIG. 80.—CRENATED RED BLOOD-CORPUSCLES.—(*Landois*.)
Often seen in improperly fixed blood slides, in freshly drawn blood after prolonged study under the microscope, in urine, etc.

(2) *Large Lymphocytes*.—Cells, several times as large as the red blood-corpuscles, with an oval or elliptic nucleus and a relatively larger amount of ungranulated protoplasm.

(3) *Transitional Leukocytes*.—Cells which resemble the last variety, but have indentations and irregularities in the nucleus.

(4) *Polynuclear*, or *Polymorphonuclear*, *Leukocytes*, or *Neutrophiles*.—These are about the same size or slightly smaller than the last variety. The nucleus is a long, deeply staining body, which is bent and twisted upon itself into irregular shapes. The protoplasm of these cells is filled with granules, which are stained, not alone by acid or basic coloring matter, but also by a combined fluid.

(5) *Eosinophiles*.—So called on account of their affinity for eosin; are about three times the size of a red blood-cell, and contain large, highly refractile, fat-like granules, which have an affinity for acid-coloring matters.

(6) *Basophilic Mast Cell*.—The granules do not stain by

Ehrlich's method, but by method given above. Has polymorphous nuclei.

In normal blood these cells occur in a definite proportion to each other: Lymphocytes, 15 to 30 per cent.; mononuclear and transitional forms, 4 to 8 per cent.; polynuclear, 65 to 80 per cent.; eosinophiles, 0.5 to 4 per cent.; mast cells, 0.25 to 0.5 per cent.

Myelocytes, not present in normal blood, are stained by the Ehrlich stain given above. They are spheric cells with

FIG. 81.—PLASMODIUM MALARIÆ. NON-PIGMENTED AMEBOID FORMS.

FIG. 82.—PLASMODIUM MALARIÆ. PIGMENTED AMEBOID FORMS.

FIG. 83.—PLASMODIUM MALARIÆ (EXTRA-CORPUSCULAR BODIES).

large, rather irregular nuclei, palely staining, and surrounded by neutrophile granules.

Blood-plates can be demonstrated in the blood when freshly drawn by the addition of a preservative fluid, such as Hayem's solution, which has the following composition:

Sodium chlorid,	2.0 parts.
Sodium sulphate,	5.0 parts.
Corrosive sublimate,	0.5 parts.
Water, distilled,	200.0 parts.

Two drops of this solution added to one drop of freshly

drawn blood, and examined with one-twelfth oil immersion lens and small diaphragm. The plates are slightly oval or rounded granules, one-third the size of a red corpuscle.

Malarial organisms (corpuscles of Laveran) should be searched for before, during, and after the malarial paroxysms by the method given above for the examination of fresh blood.

The organisms appear as small, pigmented, intracorpuscular bodies, and, at a later stage, as rosette and crescentic forms, and others as small, extracorpuscular bodies, which, under certain conditions, may develop flagella. To stain and mount see above. (For description see "Animal Parasites.")

Tubercle bacilli, found occasionally in the blood in acute miliary tuberculosis, are stained the same as in sputum.

Anthrax bacilli are rarely found in blood, but can be seen without staining, or they may be stained in carbolfuchsin.

Bacillus of Typhoid Fever.—Rarely found in the blood. Spreads are made as described above for dry method, fixed, and stained. (For technic of examination, staining, etc., of bacteria, see article on "Bacteriology.")

Spirillum of Relapsing Fever.—Prepare a slide of blood when the patient is about to have an attack, and examine with $\frac{1}{12}$ of an inch objective. (For description and technic of examination see article on "Bacteriology.")

Filaria Sanguinis Hominis.—Obtain slides of blood from finger of patient, preferably at twelve o'clock at night, and examine quickly.

The embryos are about 200 μ ($\frac{1}{125}$ of an inch) in length, and have a rapid, snake-like movement.

Dry preparations are made in the usual way,—except that no heat can be used at any time in the process,—and stained in one-half of one per cent. eosin solution in water.

Gower's Hemoglobinometer.—This apparatus consists of two glass tubes of exactly the same size; one contains a standard solution of the tint of a dilution of 20 c.mm.

of blood in 2 c.c. of water (1 : 100).* The second is graduated into 100 degrees, and is arranged to contain 2 c.c. (100 times 20 c.mm.), or more, where the percentage of hemoglobin is above 100.

Twenty c.mm. of blood are measured by the capillary pipet. This quantity of blood to be tested is ejected into the bottom of the graduated tube, a few drops of distilled water being first

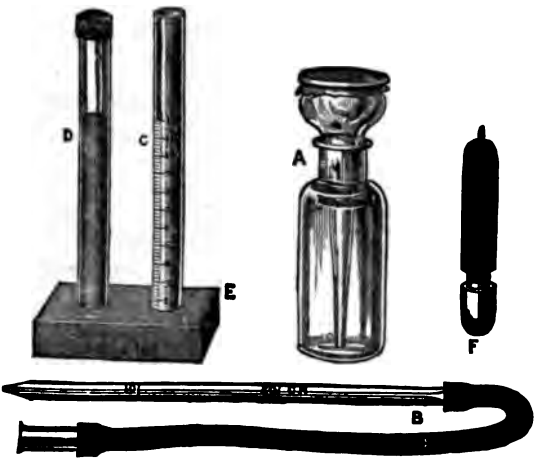


FIG. 84.—GOWER'S HEMOGLOBINOMETER.

A. Bottle for distilled water. B. Capillary tube for measuring the blood. C. Graduated tube for diluting the blood. D. Standard comparison solution. E. Base for supporting the tubes. F. Needle for pricking the skin. The instrument is no longer made as shown in the cut; the tubes C and D are now made elipsoid on section, so as to give two nearly flat surfaces for comparison. The improvement has increased the reliability of the instrument; it is not, however, so reliable as Von Fleischl's instrument, but costs much less.

placed in the latter. The mixture is rapidly agitated by a rinsing movement, and distilled water is then added, drop by drop, until the tint of the dilution is the same as the standardized tube. The degree of dilution indicates the amount of hemoglobin, and may be read off the graduated tube.

*Truly this represents a dilution of 1 : 110, but, as allowance is made in the graduated tube for this error, it is a matter of no real importance.

Von Fleischl's Hemoglobinometer.—The standard of comparison in this instrument is an elongated wedge of glass, tinted with Cassius' golden purple, and mounted movably beneath a platform like that of a microscope. In the center of the platform is a circular opening through which the light from a candle or lamp is reflected upward from a disc of plaster of Paris.

The wedge of glass underlies one-half of the circular opening

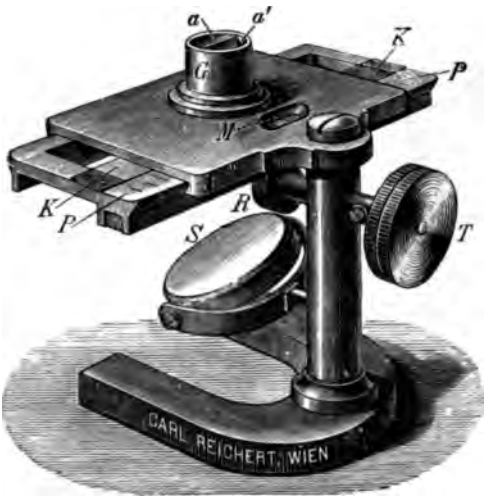


FIG. 85.—VON FLEISCHL'S HEMOGLOBINOMETER.

G. Mixing cell, divided by a partition into two chambers, *a a'*, the former receiving the blood. *K, K.* Glass wedge. *M.* Point where reading is taken. *T.* Milled head which moves the head *R*, which in turn moves the carriage *P, P*, carrying the tinted glass wedge. *S.* Disc of plaster of Paris for reflecting the light upward through the glass wedge and the mixing chamber.

in the platform. Above the wedge, and exactly over the circular opening, rests a metallic tube, 1½ cm. long, with a vertical metallic partition and a glass bottom. One-half of the tube overlies and receives its light through the wedge. This half is filled with distilled water, and in the other half is placed the mixture of blood and water. The blood is received from the finger

way between the cover-glass and the external rim. Examine with ¼-inch objective. Find number of corpuscles in at least 20 squares; divide this by 20 to find the number in a single square, and multiply the result by 4000 ($\frac{1}{4000}$ c.mm. being the contents overlying a square), and this figure by 100, the degree of dilution, and the result will be the number of blood-corpuscles contained in one c.mm. of blood.

Counting White Corpuscles.—To count the white corpuscles in a dilution such as used for the red would require more time and a much larger ruled space than is available in the Thoma-Zeiss instrument. For this reason a lower dilution is used,—1 : 10, instead of 1 : 100,—and, for diluting, a 0.33 per cent. solution of acetic acid, which destroys the red blood-cells and makes the white more distinct. The method, with the above exceptions, is as given for the red; in the calculation, however, after multiplying the number in one square by 4000, the final result is attained by multiplying by 10, the amount of dilution, instead of 100, as in estimating the reds.

Differential Counting.—Dried and fixed films are stained by Ehrlich's stain, and mounted as directed above. Then the leukocytes are counted by traversing in straight lines the whole of a cover-glass, and counting at least 1000 leukocytes. A mechanical stage greatly facilitates the count. On a piece of paper by the side of the microscope are arranged columns, at the top of which are written the forms of leukocytes; after counting the required number, each column is added up and the percentage calculated.

Differential counting of diseased red cells is sometimes resorted to, and may be done in a manner similar to the above.

Hematocrit.—This instrument readily enables one to estimate the volume of the red corpuscles. It consists of:

(1) Two glass tubes, 50 mm. long, with a lumen of 0.5 mm., and graduated into 100 parts.

(2) A metallic frame, in which the glass tubes are fastened; on the outer side by a metallic cup in the frame, and at the proximal extremity by a spring, which is attached to a hollow metal cylinder, which projects downward from the center of the frame, by means of which the frame can be made to rotate on a vertical axis.

(3) A vertical support, which can be made to rotate. A speed of at least 10,000 rotations per minute is necessary.

(4) A metallic box, fastening to a table, and containing the machinery by which the vertical support is made to rotate.

A graduated tube is filled with blood by means of a medicine dropper attached by a rubber tube, and is then securely fastened in the horizontal metallic frame and revolved for two minutes, making 10,000 revolutions per minute. The red blood-corpuscles will collect in the distal extremity of the tube, the leukocytes in the center, and liquor sanguinis in the proximal portion. Find the number of degrees the red cells occupy, and, as each degree has been found to approximately represent 100,000 per c.mm., the addition of five ciphers gives the number of red cells per c.mm. Thus, if the red cells occupy 50 graduations on the scale, there are 5,000,000 red cells per c.mm.

Widal's Test for the Diagnosis of Typhoid Fever.*—*Culture Employed.*—The culture used in the Widal test should be taken from an agar-agar growth which has been allowed to develop at ordinary room temperature for at least twenty days. From this agar-agar culture inoculations are made into tubes containing neutral beef bouillon, and the latter, after

* This description of the method has been abstracted by Dr. J. C. Da Costa, assistant in clinical microscopy, Jefferson Medical College, from his article in the *New York Medical Record*, August 21, 1897, in which he reports an examination of over 100 cases, and also an analysis of the literature on the subject up to the date of publication. I am also indebted to Dr. Da Costa and the publishers of the journal for permission to use the accompanying illustrations.

incubation at 37.5 ° C. for from eighteen to twenty-four hours, are used in the test. Instead of making bouillon growths, emulsions in sterile distilled water may be used with good

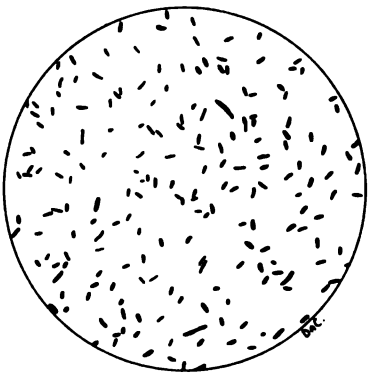


FIG. 88.—BACILLUS TYPHI ABDOMINALIS.
The bacilli are actively motile throughout the field.

FIG. 89.—A POSITIVE REACTION.
Large clumps of motionless bacilli separated by open spaces. The few bacteria outside the clumps are devoid of motility.

results by thoroughly mixing a bit of the agar growth with about 2.5 c.c. of sterile water in a test-tube until an even cloudiness is noticed.

The precautions indicated above must be followed to avoid certain false or pseudoreactions, which sometimes occur when normal blood, and blood from individuals suffering from diseases other than enteric fever, is added to a virulent culture of the typhoid bacillus.

Method of Conducting the Test.—The blood is obtained by puncture of a finger, and three separate drops are allowed to fall upon the surface of a perfectly clean glass slide which has been passed through a flame and cooled just before use. The

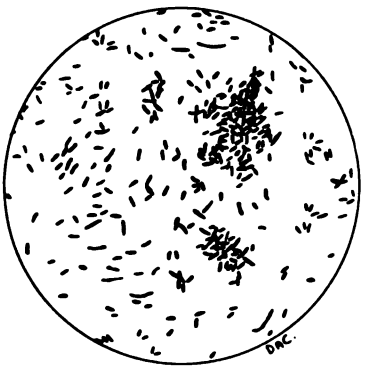


FIG. 90.—A PSEUDOREACTION.

A few small clumps of bacilli having impaired motility. Persistent motility of the bacteria in other parts of the field.

glasses are permitted to dry, and are then placed in a box to await examination at a convenient time.

To one of the blood drops a large drop of sterile distilled water is added to effect a solution of the dried blood, and while this is going on the other preparations for the test are being made, by cleaning and sterilizing by the flame two cover-glasses and a "concave slide," to be used for the microscopic examination of the specimen.

On one of the cover-glasses are now placed six drops of the

typhoid bouillon, and to this is added a large drop taken with a platinum loop from the summit of the blood solution, and the whole thoroughly mixed together. From this mixture of blood solution and typhoid bouillon a minute quantity is now placed with a platinum needle upon the center of the second cover-glass, which is immediately inverted over a hollow-cell slide, sealed with either vaselin or cedar oil, and examined under the microscope with a ⅛-inch dry objective.

Appearance of the Reaction.—If the reaction is positive, the observer will see large clumps of motionless, agglutinated bacilli, which appear as irregularly-shaped islands, separated by open spaces containing, perhaps, a few isolated bacteria, whose power of propulsion is either decidedly inhibited or entirely lost.

If the reaction be negative, the bacilli will appear as actively motile rods, darting across the field in every direction, and showing no tendency to form into masses, although occasionally small clumps of the micro-organisms may be noted. In negative reactions, however, clump formation never progresses to any marked degree, and motility persists, regardless of the time during which the specimen is watched. If any doubt exists as to the nature of a reaction, a "control" slide should be prepared with normal blood and typhoid bouillon, for purposes of comparison.

The time required for the completion of a reaction varies, but in a general way it may be said that typhoid blood will cause definite clumping and loss of motility of the typhoid bacilli within thirty minutes in the great majority of instances. In some cases a much longer time will be necessary before a correct interpretation of the test can be arrived at. *A reaction may not be classed as positive unless both clump formation and loss of motility coexist, and those reactions in which either of the phenomena are wanting may not be called typic in any sense.*

QUESTIONS.

(1) What points are determined by blood examination? (2) Give technic for the examination of freshly drawn blood. (3) How "fix" blood? (4) Give methods for staining blood. (5) What forms of red cells may be found in the blood? (6) What forms of white blood-cells may the blood contain? (7) Which of these occur in the normal blood, and in what percentage? (8) How demonstrate the blood-plates? (9) How examine for the parasites of malaria? (10) What animal parasites occur in the blood? (11) Describe the instruments used for determining the quantity of hemoglobin and their methods of use. (12) What is meant by the percentage reading of the hemoglobin? (13) How estimate the number of cells in the blood, and what is meant by differential counting? (14) What is the hematocrit, how is it used, and what information does it afford? (15) Describe the method for applying Widal's test for the diagnosis of typhoid fever. (16) Describe (*a*) the reaction, and (*b*) the pseudoreaction.

PART II.

GENERAL PATHOLOGY.

GENERAL PATHOLOGY.

CHAPTER I.

General pathology has to do with those variations in structure and function which may attack any organ. It is the study of morbid processes independent of their location, while **special pathology** is the study of diseases of organs independent of the same disease occurring elsewhere than in the organ under consideration.

By **development,** pathologically, we mean the growth of tissue into organs,—the proliferation or production by arrangement or otherwise of a tissue not identical with that from which the original cells arose; thus, in the development of the fetus, certain cells give rise to different organs—the alimentary canal, including the pancreas and the liver, arises from cellular elements which are identical. These organs are not produced by mere growth, but are dependent upon the process of development.

Growth is the increase in size of an organ by proliferation of its normal cellular units; theoretically, with a single liver lobule a whole liver could be produced by the mere process of growth.

Our knowledge of the **normal** is obtained by studying a large number of individuals or organs not manifesting disease, and considering as normal that condition which is commonest. Any deviation from this normal must come under one of three heads—*malposition*, *malformation*, or *disease*.

(1) **Malposition** is the misplacement of an organ from that

position in which it is most commonly found, or any alteration of its relation to other organs. A heart may be rotated on its axis and not occupy the normal relation to the surrounding tissue, and still the heart may be in place; so that malposition implies that the organ is either not in place, or that, being in place, its parts do not bear their normal relation to surrounding structures themselves normally placed.

Malpositions may be **congenital** or they may be **acquired.** Congenital forms are by no means always permanent, although they usually are. The acquired forms are less likely to be so, although, if they persist, such changes may occur as to render them incapable of resuming normal positions and relations. Hernia may be congenital or acquired, and in either case may become permanent through adhesions, inflammation, etc. A heart may be pushed to the right side by a left-sided hydrothorax, to return to its normal position with the subsidence of the causative lesion. If the heart be transposed with other viscera during intra-uterine life, the position assumed becomes permanent, although the organ may in no wise be diseased.

(2) **Malformation** is a deviation in structure or in development from that which is most commonly found. A malformed organ may not be a diseased organ, so that malformation, like malposition, is not of necessity disease; as to whether it was brought about by previous disease or not, is a question which can not always be determined; so that a malformation may be maldevelopment, or it may be acquired as the result of disease; just in the same way we may have acquired malpositions. Acquired malformation is most commonly known as deformity, *e. g.*, the deformity following fractures, accompanying dislocations, or due to tumors or swelling.

(3) Morbid processes induce or are expressions of **disease,** and this disease may be manifested as a **disease of structure** (**organic disease**) or **disease of function** (**functional disease**). It is probable that there is always a lesion of structure in

order to produce a lesion of function, and that the so-called functional diseases, such as palpitation of the heart, are due to changes in the innervation, temporary in character, and brought about by stimulation or depression by chemical elements circulating in the blood or arising in organs, such elements not being a part of the normal chemistry. Disease of structure usually means disease of function; but the fact that tissue is supplied in excess of the common demands of organic life leaves room for considerable loss of structure or modification of tissue without apparent alteration in function. If reduced to its last analysis, we may define disease as any tissue alteration or structural change which alters the function of the integral elements of which a tissue or organ is composed, such alteration of function being beyond the limits of that which is normal.

Pathogenesis or Cause of Disease.—Whatever may be the changes going on in an organ or tissue, we must believe that it has a cause, and that the manifestation which we recognize as disease represents the reaction of the normal to some influence: some entity, either known or presumed. Like all other manifestations of force (whether it be light, or heat, or the activity of cells depending upon those cell changes which we recognize as nutrition,—conversion of force or energy by chemic changes), they all must have some starting power, some cause. This cause so enters into the process that it is a most important part, and therefore the study of disease implies a knowledge of its cause. The acting cause induces a certain perversion from the normal, which constitutes the morbid process, and this marks its pathway by results. So the study of disease implies a study of **cause,** the effect acting, and **result,** or the **effect terminated.** So far as its influence on life is concerned, the result may be more disastrous than the active process. As an example of this fact, we observe a gumma of the larynx, in which the most obstinate symptoms

manifest themselves after the absorption and cicatrization of the lesion begins, and the stenosis of contracting fibrous tissue threatens life by occlusion of the air passage.

The study of the active process associated with disease and its results implies a study of the gross alterations, the **morbid anatomy,** and, what is truly included as a part of the anatomy, the changes in the finer structure of the tissues, the **morbid histology.** That the study of these two divisions of the subject shall have important bearing on practical medicine, we must observe the relation maintained between both gross and microscopic lesions and the function of the diseased organ ; this is a study of the **morbid physiology,** the perversion of the normal, due to, or associated with, the lesions, either gross or microscopic, which constitute the active phenomena of disease.

Hypertrophy may be defined as increased functional power which has a tendency to persist, and which is beyond the normal for a given tissue under its existing conditions; thus, a heart weighing 12 ounces may be normal for the adult, but would be hypertrophic in a child. Hypertrophy is not increased size, *e. g.*, the amyloid liver may weigh six kilos and be functionally inactive. The above definition also excludes tumors, which perform no function. Hypertrophy is usually associated with abnormal size and weight, but not necessarily. Hypertrophy must be differentiated from the so-called **reserve force of organs** ; thus the heart, during a period of intense excitement, may perform effectually two or three times the work which is normal for it, and still the organ may not be hypertrophied. The condition, however, does not persist ; it is temporary.

Causes of Hypertrophy.—Increased work with supplied nutrition are the causes most active in extra-uterine life. These, however, fail to account for certain enormous overgrowths of organs or tissues which occasionally occur. Thus,

general or partial **giant growth** may arise without any apparent extra demand for work, although, of course, the extra nutrition is supplied. This phenomenon (giant growth) has been alleged to arise from **congenital impulse**—an expression which only moves our ignorance of the actual cause back to a period of which we know but little as to the functions of organs. Since we have come to appreciate the fact that many organs perform functions of nutrition, heat production, etc., it is to be conceived that some extraordinary call has been made upon them, the nature of which we can not in the present state of our knowledge estimate; this extra call may constitute the demand for additional tissue, and hence hypertrophy. There can be no apparent reason for an enormous hypertrophy of the facial and long bones, as is sometimes seen, but there must be some reason for the change, and whether this be attributed to changes in innervation, or to unusual demand for some functional activity which we can not estimate (such as blood making by the marrow), remains to be further studied. The two conditions—supplied nutrition and conversion of the added nutrition—are necessary; if work be increased without sufficient nutrition, wasting occurs; on the other hand, nutrition may be abundant and, without work, the tissue may waste; as an example of the latter, we have the wasting of the muscles of the arm when splinted for the treatment of fracture—the nutrition may be just as abundant as when the organ is uninjured. Hypertrophy is sometimes said to be true or false—the latter is not possible. The term false, or **pseudohypertrophy**, is applied to large organs in which the increase in size is not attributable to increased functional power or to increase of the elements in the normal proportions, but rather to increase in size due to the invasion of tissue by a new element, overgrowth of some existing tissue, or some similar condition. The enlargement of the liver, associated with amyloid disease, fatty infiltration, or red atrophy, may be taken as types of

so-called pseudohypertrophy. The term is a bad one and should not be used. Hypertrophy is said to be **simple** and **numerical**; by the former is meant an increase in the size of the cells, and by the latter an increase in the number of cells.

Physiologic hypertrophy differs from other forms of hypertrophy in that it anticipates the increased work which may be demanded of the tissue. In a certain sense, all forms of hypertrophy are physiologic; hypertrophy is not a disease; but the condition referred to as physiologic hypertrophy is typified in the enlargement of the mammary glands and the increase in muscular power of the uterus in anticipation of lactation and labor. Unlike all other forms of hypertrophy, this condition apparently arises independent of existing increased work; as far as our knowledge goes, it anticipates such work.

Hypertrophy is said to be **compensatory** when one organ performs the work of another; thus, if one kidney be diseased, the opposite organ may undergo hypertrophy; if one lobe of the liver be destroyed by disease, the remaining lobes may be increased in size. Compensatory hypertrophy develops with more certainty in the young, while in extreme age the tissues fail to respond to demands made for additional work.

Limitations of Hypertrophy.—If the occurrence of hypertrophy depended entirely upon the demand for work, there is no reason for it not indefinitely progressing. Experience, however, shows that a point is always reached, sooner or later, when compensation fails, and work demanded beyond this point leads to wasting. As remarked above, the older the individual the earlier this occurs—a fact which suggests that the blood-vessels are responsible, to a certain extent, for the arrest of the process. It is observed in athletes that, if a man has thoroughly trained early in life, he remains competent of training into "condition" throughout the major part of his days. Early in life the blood-vessels are competent of increasing their carrying capacity more than in later years—a fact

very well known of the arteries. This enables us to see another reason, beside the active tissue growth of the young, which enters into the explanation of hypertrophy, in some cases being greater than in others.

Theoretically, once an organ begins to hypertrophy there is no reason for the process not being indefinite ; but a stage is eventually reached when the blood supply is no longer competent, the arteries being inadequate or unable to transmit the demanded additional blood. When this stage is reached, not only is hypertrophy arrested, but, if the demand be continued, wasting occurs ; clinicians recognize, in the treatment of heart diseases, that, even with well-established hypertrophy and good nutrition, a stage is reached where the best results are attained by diminishing the demand for work rather than lashing an already overworked organ and hoping for continued hypertrophy.

Hyperplasia is an increase in the connective tissue of an organ, either associated with or independent of increase of the elements upon which the functional activity of the organ depends. If there be an increase of the functionally active cells of the organ, the increase in connective tissue must be in excess of that which is normally present, in order to be a hyperplasia. The term hyperplasia is also applied to disproportionate increase in any element of an organ. Thus, a new growth of bile-ducts is spoken of as hyperplasia; newly developed gland-cells, or an excess of one constituent of an organ without corresponding growth of the other elements, is spoken of as hyperplasia.

Metaplasia is the direct transformation of a tissue into a dissimilar tissue. This is only possible of tissues of the same type. Different forms of epithelium changing one into another, or one connective tissue converted into another, as cartilage into bone, or fibrous or loose connective tissue into fat. Transposition of type is not possible : epithelium never

becomes connective tissue, nor is connective tissue ever converted into epithelium. An ulcerative process in the trachea, after cicatrization, is covered by flat epithelium from the genetic layers of adjacent columnar epithelium, the process being known as a metaplasia. That it be a pure metaplasia there must not be the intervention of embryonic tissue. Theoretically, such a thing is possible, but whether actually a cylindrical cell is ever converted into a squamous cell, without the intervention of practically an embryonic cell, seems somewhat doubtful.

Heteroplasia implies the production of a tissue in an organ when such a tissue, which may be perfectly normal elsewhere, is not a normal constituent of the organ in question. The development of cartilage or bone in certain glandular structures, such as the parotid, ovary, or testicle, constitutes a heteroplasia. The best type of heteroplastic tissue is a tumor of the typic series.

Atrophy is the reverse of hypertrophy, and hence is diminished functional power, which has a tendency to persist or increase, and which is associated with structural alterations in the tissue involved. It is not merely diminished size or weight, as, in the condition known as red atrophy of the liver, the organ may be much increased in size. Atrophy is not an arrest of development. Atrophy occurs in developed tissue, although the arrest in development may be followed by atrophy of that tissue which has already developed.

Causes.—Atrophy may be *physiologic; e. g.*, atrophy of the uterus after labor, atrophy of the sexual organs after the menopause. Atrophy may result from *pressure*, as the pressure atrophies of the liver. *Disuse* of a tissue will lead to its gradual atrophy. This is the type of atrophy which leads in generations to the disappearance of tissues and organs no longer used. The wasting incident to the fixation of a limb in the treatment of fracture is in part due to the disuse, and

also, in many cases, the pressure of dressings. *Inanition* or faulty nutrition, whether general or local, will give rise to atrophy; as examples of general atrophy due to inanition we have the progressive muscular wasting which occurs in consumption, the cachexia of malignant tumors, and in profound blood dyscrasiæ. Certain atrophies are spoken of as *trophic; e. g.*, atrophy associated with disease of the anterior cornu of the spinal cord; unilateral neuropathic atrophy of the face. *Inflammatory processes* may lead to atrophy by pressure and by interference with the nutrition.

In the cells and tissues involved in atrophy there is general shrinking of the diseased structures; the cells become granular and not uncommonly pigmented; it is probable that in this granular or fatty condition absorption of the cells is readily possible; certainly functional activity is enormously diminished, if not in advanced cases suspended.

This association of structure change with absorption and disappearance of cells has led to the name **degeneration atrophy.** It is probable that all atrophies are associated with some degenerative phenomena in the cells; by no other means can we explain the disappearance of structure. It is held, however, that atrophy is possible without appreciable cell change; such a condition has been termed **simple atrophy.** Again, when the atrophic phenomena are due to the inability of the cell to assimilate supplied nutrition, the lesion is said to be an **active atrophy**; when the fault lies in deficient nutrition it is called **passive.**

Hypoplasia differs from atrophy in that development has been arrested either before or after birth; it is not the wasting of tissue, but the failure to reach the normal development. The process may involve the whole body, or may be restricted to one or more organs or parts of organs. Dwarfs are examples of hypoplasia. When the process is not universal, but is restricted to one side of the body or an organ, as the brain, it is spoken

of as **asymmetric hypoplasia.** The cause may lie in incomplete development, or partial occlusion, of the blood-supply to the tissues involved. This not rarely proves to be the case where syphilitic endarteritis has lessened the blood-supply to an organ, or part of an organ; the former is sometimes seen in the liver, and the latter in the kidney. The environments of organs may lead to hypoplasia, as when bands of inflammatory tissue restrict the growth of organs, or failure of development of the skull limits the growth of the brain.

Agnesia or **aplasia** should be restricted to mean entire failure of development: that there has been no effort at the production of an organ or tissue. This is seen in the kidney at times, and is usually due to obliterative disease of the renal artery. The term is also applied to the disappearance of partly developed organs. It is also used to indicate the failure of a given structure of an organ to develop. As examples of the latter, occasionally the fibrous tissue of an organ develops without any corresponding development of the parenchyma, in which case there is said to be agnesia of the parenchyma.

QUESTIONS.

(1) What is general pathology? (2) What is special pathology? (3) What is meant by development and growth? (4) How do we obtain our idea of the normal? (5) What is meant by malposition, and what are its forms? (6) What is deformity? (7) What is malformation? (8) What is meant by (*a*) functional disease, (*b*) organic disease? (9) What is meant by pathogenesis? (10) What is meant by morbid anatomy? (11) What is morbid histology? (12) What is morbid physiology? (13) What is hypertrophy, and how does it differ from the reserve force of organs? (14) Give causes of hypertrophy. (15) What are the forms of hypertrophy? (16) How does physiologic hypertrophy differ from other forms? (17) What is meant by the limitations of hypertrophy? (18) What is hyperplasia? (19) What is metaplasia? (20) What is heteroplasia? (21) What is atrophy, and give causes? (22) Give an example of atrophy arising from each of the causes enumerated. (23) What is meant by active atrophy? (24) What by passive atrophy? (25) What is meant by hypoplasia? (26) What is agnesia or aplasia?

CHAPTER II.

INFILTRATION AND DEGENERATION.

(*a*) **Infiltrations.**—*Infiltration* is the "filtering-in," or deposition in organs, or the addition to organs, of elements not normally present, or an excess in quantity of a material which is normally present. It will be observed that the term "infiltration" is here applied to a material and not a tissue, although one must confess that the difference is not striking. If tissues are included as infiltrating bodies, then a tumor invading an organ would be an infiltration; such is not the meaning of the term in the sense here used. The materials studied in the infiltrations are chemic bodies, rather than bodies with definite histological structure. Thus fat, lime salts, the various pigments, glycogen, and even amyloid material, are bodies with definite chemic composition, and not composite mixtures of many agents, as are the tissues. It is true that amyloid material has a rather characteristic histologic structure and stain reaction; so have many crystals, but this does not make them tissues in the common acceptation of the term. Infiltrations are (1) fatty; (2) amyloid or albuminoid; (3) pigmentary; (4) calcareous; (5) glycogenic.

(1) **Fatty infiltration** consists in the addition of fat to an organ in which fat is not normally present, or the addition of a large amount of fat in an organ which normally contains less.

Causes.—Increased nutrition; decreased work; slowed circulation. In the increased nutrition fat is stored in the cells, being in excess of the quantity which the cells can utilize for existing demands. If the functional activity of the cell be reduced by lessened demand, and the normal amount of blood

is sent to the cell, the nutrition is in excess, and fatty infiltra-

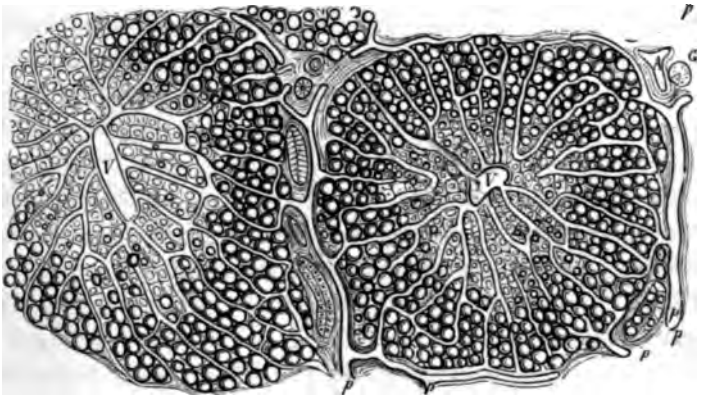


FIG. 91.—FATTY INFILTRATION OF THE LIVER. SEMIDIAGRAMMATIC.

V. Hepatic vein. *p.* Portal vein. *A.* Hepatic artery. *G.* Bile duct. The globular cells loaded with fat are seen in the periphery of each lobule.—(*Rindfleisch.*)

tion may result. Moderate slowing of the circulation gives rise to fatty infiltration; thus slowing of the circulation partly accounts for the fat infiltrated into the connective tissue of the omentum and mesentery in cirrhosis of the liver, and also for the fatty infiltration which occurs in the liver lobules in cirrhosis.

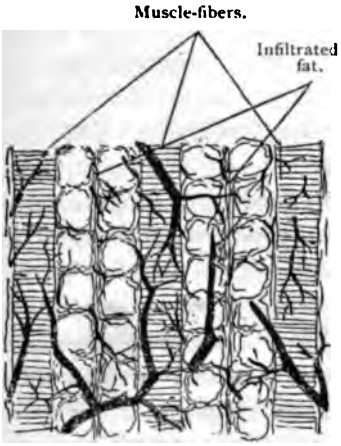


FIG. 92.—PSEUDOHYPERTROPHIC MUSCULAR PARALYSIS; FATTY INFILTRATION OF MUSCLE.—(*Flütterer.*)

Sites.—In the liver, particularly in the peripheral zone of the liver lobule; general subcutaneous tissues, with the exception of the lax areolar tissues of the scrotum, eyelids, lips, alæ of the nose and ears; in the connective tissue between the muscle-fibers, pseudo-

hypertrophic muscular paralysis, and in other connective tissues.

Microscopically, the fat is taken up by the connective tissue cell; the nucleus is crowded to one side, the fat existing in the cell as a single large fat-globule; in the liver tissue the fat is taken directly into the liver cell. The nuclei of the infiltrated cells are not diseased, but merely show crowding to one side. In the muscular tissues the fat is infiltrated between and not into the muscle-fibers, a condition easily differentiating fatty infiltration from fatty degeneration.

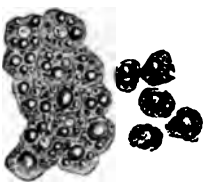


FIG. 93.—LIVER CELLS SHOWING FATTY INFILTRATION. × 250 diameters.—(*Schmaus.*)

(2) **Amyloid** or **albuminoid infiltration,** also known as **albuminoid disease, lardaceous infiltration, waxy** or **bacony infiltration.** This product is found during health in the prostate gland, and has been observed in the pia mater.

Causes.—Amyloid material probably represents an altered fibrin, and can be made artificially by suspending the spinal cord in alcohol for a few months. The artificial product so made answers all the stains for amyloid, and can not be differentiated from the natural material. If fresh blood be whipped, the fibrin withdrawn, washed, and treated with a 1 : 2000 solution of hydrochloric acid, the mass becomes gelatinous, clear, and pultaceous, and answers all the stains for amyloid material. As amyloid infiltration most commonly occurs in connection with long-standing suppuration in which the alkaline salts are drained in excess, and as the product resembles a de-alkalinized fibrin, it was supposed that the disease process naturally arose as a result of the removal of alkaline salts from the blood; this is not borne out, however, by the fact that amyloid infiltration occurs in malaria and syphilis, very often where there has been no suppuration. Tuberculosis is often the cause,

especially bone and lung tuberculosis; anything which greatly reduces the general nutrition favors its development.

By some amyloid disease is regarded as a degeneration. In a sense this is true; in the blood the alteration is of the nature of a degeneration; the material itself is a degeneration product, as, probably, is melanin. As deposited in organs, it represents an additional element,—an infiltration; and as the degenerative process is restricted to the origin of amyloid

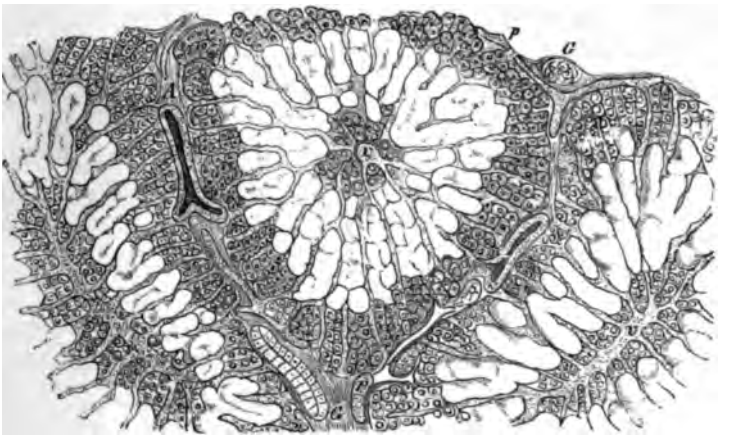


FIG. 94.—AMYLOID LIVER. SEMIDIAGRAMMATIC.

A. Branch of hepatic artery with amyloid walls. *G*, *G*. Bile ducts. *P*, *P*. Portal veins. *V*, *V*. Hepatic veins. The colorless area occupying the intermediate zone of the liver lobules is amyloid material.—(*Rindfleisch*.)

material, the term infiltration is applied to the deposit in organs and tissues. There is not adequate proof that, where found, it results from a degenerative change in the tissues at hand; *e. g.*, it is not probable that the amyloid liver weighing 7 kilos is the result of a degenerative change in an organ normally weighing 2.5 kilos.

Sites.—The process usually begins in the blood-vessels, deposition taking place in the intima and between the intima

and adventitia, displacing, to a certain extent, the muscular coat; this occurs almost exclusively in the arteriole, but may be seen around the capillaries, and occasionally in the larger blood-vessels. The organs most commonly involved are the liver, spleen, kidneys, mucous membranes,—more particularly those of the intestines,—and the lymph-glands.

Morbid Anatomy.—The organ is large, heavy, and pale, the paleness being due to the infiltrated material and to the anemia; the borders of the organ are rounded; it is tough in texture; decomposition takes place very slowly; the organ possesses a specific gravity very much higher than the normal. In the spleen, the Malpighian bodies are largely involved, and usually show as small translucent grains, resembling boiled sago, and hence the name "sago-spleen." (For description of morbid anatomy of albuminoid infiltration of the liver, see chap. IX, part III.)

Chemic Tests and Reactions of Amyloid Material.—With a watery solution of iodin, made by the addition of iodid of potassium,* the amyloid material is stained a mahogany brown. If this test be made in the presence of dilute sulphuric acid, occasionally a blue color will be obtained, and this led Virchow to believe that the material was starch-like, and hence called amyloid; the sulphuric acid and iodin test is less satisfactory than the iodin test alone. If the tissue be treated with methyl-violet or gentian-violet, the amyloid material will stain a rose-pink color, and the surrounding tissues purple or blue; this stain is largely used for microscopic purposes; the stain is used in two per cent. aqueous solution, sections washed in water, and mounted in glycerin jelly. Amyloid material is not digested by pepsin, is soluble in ammonia and in strong hydrochloric acid; is not soluble in acetic acid or dilute mineral acids.

* See "Gram's Fluid" chap. VIII, part II, "Bacteriology."

(3) **Pigmentary infiltration,** also known as **pigmentation,** consists in the introduction into the tissues or cells of pigment granules. These pigment granules may arise from two sources: (*a*) They may be imported into the body, and are therefore **extraneous pigments,** or (*b*) they may arise as the result of changes in elements normally present in the body,—**autochthonous pigments.** Another form of pigmentation, known as **pseudomelanosis,** has been described; it is essentially due to hydrogen sulphid coming in contact with

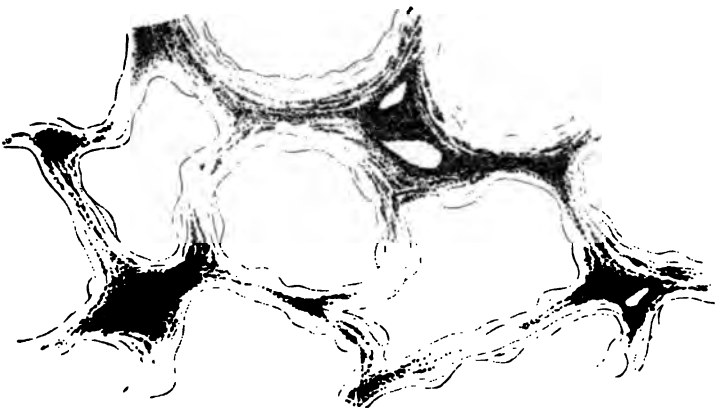


FIG. 95.—SECTION OF LUNG SHOWING INFILTRATION OF THE CONNECTIVE TISSUE OF THE ALVEOLAR WALL BY COAL-DUST. ANTHRACOSIS.—(*Rindfleisch.*)

the iron present in the tissues postmortem. It is usually seen on the under surface of the liver, and occasionally on the intestines; sometimes the spleen shows it. One knowing of its presence postmortem is not likely to be misled as to the condition when seen.

(*a*) *External or Introduced Pigments.*—These are well illustrated in pneumonokoniosis. (See chap. IV, part III, "Mucous Membranes.") In this type are included solid pigments arising from external sources, such as hard coal in miners, iron in laborers in iron manufactures, and, in stone-cutters, particles of

sand. Any of these insoluble pigments can secure access to the tissue through a wound, in which they are probably retained by the action of phagocytes. A form of this pigmentation, as it occurs in wounds, is seen in tattooing, also in the small grains of powder which may be thrust into the skin in powder explosions. When the solid material is

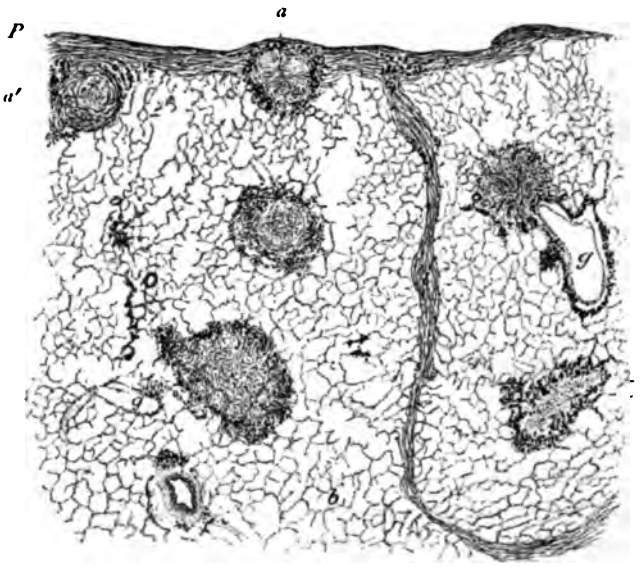


FIG. 96.—SECTION OF A LUNG SHOWING CHALIKOSIS.

P. Pleura. *b.* Nearly normal air vesicles; some are slightly emphysematous. *a.* Mass of infiltrated material with dense fibrous capsule and situated in the pleura. *a'.* Similar mass in the lung tissue; other masses are shown. *i.* Thickened fibroid, interlobular septum. *g.* Blood-vessel, around the branch of which is forming an area of infiltration.—(*Schmaus.*) × 30 diameters.

hard coal, the condition is spoken of as **anthracosis**; when the material contains iron, the condition is known as **siderosis**; when composed of sand, or fragments of stone, as in stone-cutters, it is spoken of as **lithosis** or **chalikosis.** Once the pigment passes through the protecting membrane,—either skin or mucous membrane,—it reaches the lymphatic

spaces, and may pass on to the lymph-glands, or even further, and eventually reach the circulation. A lymph-gland may break into a blood-vessel, and the solid pigment be carried by the circulation everywhere. Weigert asserts that this is a method by which any extraneous pigment reaches other viscera than the lung, *e.g.*, the liver and spleen. Other extraneous pigments do not enter the body as pigments, but are converted into pigments by the action of the body juices. Silver may be taken as a type of these pigments entering the circulation and coming to the surface of the body as an albuminate. It is deposited in the skin by the action of light, as metallic silver, the resulting condition being known as **argyria.**

(*b*) *Pigments Derived from Elements Normally Present in the Body.*—Pigmentation is a normal process in the skin of the negro, and in the iris, etc. Pigments derived from the blood, so-called *hematogenous pigments*, are the results of changes in the normal hemoglobin during life. In health the hemoglobin is not yielded to any of the tissues with which it comes in contact; in certain diseases, however, the blood-coloring matter may be altered, as in *hemoglobinemia*, or this hemoglobin may pass off with some of the excretions, as in *hemoglobinuria.* During life the two blood-pigments resulting from changes in the hemoglobin are *hematoidin* and *hemosiderin;* the latter differs in many respects from the former: the principal difference is that hemosiderin contains iron. A pigment very closely allied to the above is *melanin;* with hemosiderin, melanin forms the chief pigment of malaria. Melanin is a normal pigment in the skin of the negro and around the nipple in the white; it is also seen in tumors, where the condition is spoken of as *melanosis*, or the tumor is said to be *melanotic;* it may be produced by the cellular activity of the part, and it may follow hemorrhage. In Addison's disease, melanin is deposited in the skin of certain parts of the body;

in malaria, melanin may be found in the large glandular viscera, such as the liver and spleen.

When any of the hematogenous pigments are deposited in organs, the tissue affected is said to show **hemochromatosis**, a name given to the condition by von Recklinghausen. Hemochromatosis is seen in the liver, spleen, lymph-glands, bone-marrow, lungs, and kidneys, and, in very rare instances, in the mucosa of the intestine.

Jaundice.—A form of pigmentation in which the pigment is derived from blood-coloring matter, but which, at the same time, would not occur without the intervention of another process in metabolism, is jaundice. While it is true that certain blood pigments and hematoidin are chemically identical with bilirubin, and that the latter is abundantly formed when there is rapid hemolysis, still there is not sufficient reason for believing that this production is ever sufficient to give rise to jaundice. Bile pigment is produced in the liver, and by re-absorption enters the circulating blood, and is the agent which produces the discoloration of the various tissues so markedly influenced in jaundice. The pearly white of the conjunctiva is usually first to manifest the discoloration; afterward we see all of the tissues more or less discolored.

There is a form of pigment known as **hemofuscin**, seen in the heart muscle, and occasionally in unstriped muscle, having been noted mostly in the muscular layer of the jejunum. The chemic characteristic of hemofuscin is that it does not contain iron, and is, therefore, like hematoidin; its color is of the brightest red, and the granules are finer than hematoidin. Its source has not been definitely determined.

A pigment closely allied to hematoidin is *lutein*, which is the coloring-matter of the yolk of the egg, and is found in the corpus luteum.

There are a few pigments which do not enter the body as

such, but which are developed in the body from elements not normally present; as an example of these, we have the pigmentation following the administration of silver, *argyria*.

(4) **Bacterial Pigmentation.**—Certain pigments produced by bacterial growth occur in suppuration. The bacillus pyocyaneus is the organism most commonly producing pigment in pus, or even catarrhal discharges from such mucous surfaces as the nose, uterus, and, rarely, the bowels.

(5) **Calcareous infiltration** or **calcification** consists in the deposition in the tissues of salts of lime and magnesium; the lime salts are the phosphate, carbonate, chlorid, and fluorid; the magnesium salt is a phosphate.

The term **petrification** or **petrifaction** has been applied to deposits composed purely of magnesium and other than lime salts, while the term **calcification** has been restricted to lime salts. That such a sharp differentiation is advisable, or even possible, is, I think, doubtful.

Morbid Anatomy.—The lime salts may form distinct concretions, as in tubercular abscesses and tubercular glands, or they may be diffused between or into the cellular elements of a tissue, *e. g.*, the cartilages of the ribs. This latter is analogous to ossification observed in bone; calcification differs from ossification in that the former does not have any distinct histologic structure.

Causes.—Local changes in nutrition, coagulation of albumin, slowing of the circulation, inflammation, and chronic infections. Calcification is one of nature's methods of limiting infection, as is shown by the calcareous masses which collect around tubercular areas and in actinomycotic masses and in the fungus itself.

Seats.—"Healed-in" infectious processes, or where attempts at "healing-in" have been made; it also occurs in the cartilages, *e. g.*, those of the ribs; it also occurs in cicatricial tissues,

particularly those connected with the periosteum; it is seen in certain tumors, *e. g.*, psammoma of the brain, in thrombi, and in degenerative processes.

Uric Acid Deposits.—With gout is associated the abundant deposit of uric acid and its salts, particularly in connection with the joints, although the kidneys, skin, and fibrous tissues of the body are also likely to be involved. Wherever the deposit takes place there is usually a surrounding area of local necrosis, or at least marked degenerative changes. The cause of the deposits has not been definitely determined. We do not even know whether it is defective excretion, over-production, or faulty oxidation. The deposition is usually associated with local pain and inflammation. The deposits are composed for the most part of sodium urate, with a trace of phosphates and carbonates.

(6) **Glycogen Infiltration.**—Glycogen, like fat, is a normal constituent of liver tissue, arising from the metabolism of grape sugar by the extraction of a molecule of water:

Grape Sugar.		Water.		Glycogen.
$C_6H_{12}O_6$	—	H_2O	=	$C_6H_{10}O_5$

That it can also be produced from albumins there seems no reasonable doubt; but the uncertain composition of the proteid bodies makes the chemic change into glycogen from albumin an unsolved problem in physiologic chemistry. While produced normally in the organism, it is in diabetes that we see its most remarkable generation. When we have solved the pathology of diabetes, the production of glycogen, and particularly its tissue infiltrations, will become apparent. It has a rather remarkable resemblance to amyloid material, and still, that it is not the same can easily be established. It reacts with an aqueous solution of iodin very much as amyloid material, but does not give the blue with iodin and sulphuric acid; while amyloid is insoluble in water, glycogen is

freely soluble. Glycogen is converted postmortem into grape sugar. The extraction of glycogen from the liver is accomplished by dissolving it in an alkali and precipitating by alcohol. It is a white powder, freely soluble in water, giving the solution an opalescent tint.

To demonstrate glycogen in the tissues, anhydrous alcohol is used for fixation, infiltrate with celloidin, and harden in cedar oil and chloroform. For staining, Barfurth advises a glycerin solution of iodin, and Ehrlich a syrupy solution of iodin in gum acacia. By either of these solutions it stains a brown, like amyloid, but is differentiated by the insolubility of the last-named body.

As an infiltration, glycogen is found in the liver, epithelial cells of Henle's loops, in leukocytes and pus-cells, in tumors (particularly carcinoma and adenoma of the testicle), in sarcoma of bone, and, rarely, in similar tumors in other situations. It is present in the leukocytes in diabetes, and it is claimed that the diagnosis of diabetes can be made, before sugar appears in the urine, by the glycogen reaction of the leukocytes.

Morbid Anatomy.—Organs showing glycogenic infiltration resemble amyloid with the following exceptions: The specific gravity is low; there is not the bacony density; there is less anemia and brittleness; and the difference given above in the chemic stain reaction.

Cholesterin Infiltration.—There is much doubt as to this being an infiltration; in degenerative processes it is likely to be found, but gives no macroscopic evidence of its presence. Under the microscope it may be recognized as thin rhombic plates, with not very regular edges, and quite commonly a small square out of one corner, appearing as though it had been cleanly cut out. (See Fig. 72, p. 74.) In addition to the degenerative processes already mentioned, cholesterin is found in the contents of cysts, and sometimes in inflammatory exudates and in atheromatous areas.

(*B*) DEGENERATION.

Degeneration implies that the cellular elements of an organ are undergoing or have undergone such changes, both chemic and structural, as to preclude their proper maintenance of function; degeneration differs from infiltration in that infiltration is something carried to the organ or cell and deposited, or something manufactured by the cell and retained, while degeneration implies that the cell, including its chemic and physical elements, has undergone important nutritive changes which may be entirely independent of any extraneous material brought to the organ involved. Infiltration may lead to degeneration, and degenerations may be accompanied by infiltrations; the processes are, however, distinct. Degenerations are also known as **metamorphoses**; occasionally a degeneration is spoken of as a **necrobiosis**; this is not, however, correct, as the latter condition implies molecular death, and an organ may be degenerated or a cell may be degenerated, and not as yet dead. The degenerations are parenchymatous, hydropic, fatty, colloid, mucoid, and hyaline.

(1) **Parenchymatous degeneration,** also known as **cloudy swelling, granular degeneration,** and **parenchymatous metamorphosis,** consists of a precipitate, within the cell protoplasm, of what seems to be albumin in a finely granular form. The nucleus of the cell is crowded with minute granules or may be destroyed; the perinuclear protoplasm contains an abundant granular precipitate; the cell outlines are indistinct, and the entire body may be disintegrated. It is probable that the continuance of the process terminates in a fatty degeneration, and the granular bodies seen are eventually converted into oil; the cell may again be cleared up by the use of dilute acetic acid or a strong alkali. The nucleus will again become visible, although the granular bodies may merely agminate, or may disappear.

Causes.—High temperature, poisoning by carbonic, phosphoric, and arsenious acids; intense or long-continued hyperemia, vascular stasis, and edema; inflamed mucous membranes usually show it to a high degree; a similar process is seen in inflammation of muscle, *e. g.*, acute myocarditis; in acute yellow atrophy of the liver many of the cells will be found granular and many of them advancedly fatty; any malnutrition may simulate the condition, and many poorly nourished gland-cells, particularly in atrophic processes, show the change.

Morbid Anatomy.—The organ is swollen, increased in size, cloudy or opaque on its surface, softer than normal, and where

FIG. 97.—CLOUDY SWELLING OF THE EPITHELIAL LINING OF THE KIDNEY TUBULE.—(*Flütterer.*)

FIG. 98.—GRANULAR DEGENERATION OF A MUSCLE-FIBER, LAST STAGE, NEARLY FATTY.—(*Schmaus.*)

FIG. 99.—CLOUDY SWELLING OF THE LIVER CELLS.—(*Schmaus.*) × 250 diameters.

the process is simple there is evidence of anemia, but, as commonly seen, there is an increased amount of blood in the part, *e. g.*, the cloudy swelling seen in the kidney may be the initial stage of inflammation, and the organ may be distinctly hyperemic.

Termination.—If the causes be early withdrawn, it is probable that recovery of the cell may occur; if the cause continues to act, fatty degeneration ensues, the cells are destroyed, and new cellular elements must be produced by the undestroyed tissue elements or the connective tissues.

(2) **Fatty Degeneration.**—This probably represents but

a later stage of the preceding. The cells now have the granular bodies, before noted, converted into minute oil drops; the nucleus is destroyed and can not be made to reappear; the cell is shrunken and not swollen; its outlines are apt to appear irregular, or evident cell dissolution may be manifest. The oil drops do not run together as in fatty infiltration, and the cell is not cleared up by acetic acid as in cloudy swelling. The cellular debris is usually manifest; the organ diminishes in size. The compound granule cells in brain softening represent a type of fatty degenerated cells.

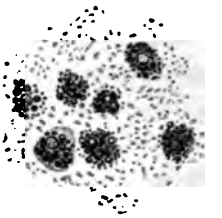


FIG. 100.—FATTY DEGENERATION OF THE LIVER CELLS.—(*Schmaus.*) × 250 diameters.

Causes.—(1) The causes already given for cloudy swelling; (2) anemia; (3) some of the forms of necrosis are accompanied by fatty degeneration, *e. g.*, caseation.

Morbid Anatomy.—As soon as the removal of fat by absorption begins, the organ diminishes in size, is pale, soft, almost pultaceous, feels greasy, and greases the knife with which it is cut. The organ is paler than normal, yellow in color, markedly anemic, and may show some interstitial or parenchymatous hemorrhage as a result of the degenerative processes in the capillaries.

Seats.—Epithelial surfaces and glandular viscera, muscles, nerves, and blood-vessels; occasionally observed in the brain, and there constitutes a variety of softening.

(See "Fatty Degeneration of the Heart, Blood-vessels, Liver," etc., part III.)

(3) **Hydropic degeneration (cellular dropsy, cellular vacuolization)** is practically a cellular edema. The affected cells are very much larger than normal, and contain many so-called vacuoles, usually in the perinuclear protoplasm, although the nucleus may be involved. The evident cell damage is less than in parenchymatous degeneration.

Causes.—Edema, inflammation, infectious processes, and degenerative lesions in general when affecting the large ganglion cells of the central nervous system.

Sites.—Epithelial surfaces, particularly the mucous membranes, glandular viscera in inflammation and edema, edema of the muscular tissues in which many fibers are swollen and, on transverse section, show extensive central vacuolization. The morbid anatomy is practically that of edema, but hydropic degeneration is often present when no gross lesion is manifest.

(4) **Colloid degeneration** is a process by which cellular protoplasm is converted into a homogeneous, gelatinous, structureless mass. The exact cause of this change is not known; it occurs in connection with epithelial cells, to which it is practically restricted. It is, therefore, a common phenomenon in glandular structures where exit is prevented by occlusion of the duct; it is seen in the kidney and in ovarian cysts; it occurs in goiter and in cancerous masses. The constancy with which it is found in the thyroid gland has led many observers to believe that it is a normal constituent of that organ, and, when greatly increased in amount, the condition is spoken of as colloid goiter. The exact chemic nature of the material has not been definitely settled; it is not precipitated by alcohol or acetic acid, it is insoluble in water, and is not rendered opaque by chromic acid.

Macroscopically, the material is gelatinous, stringy or ropy, and is usually colorless, but may be slightly bluish or yellow.

Microscopically, it will occasionally be observed to be arranged in concentric masses. It does not stain with the anilin dyes, but stains with carmin.

Colloid degeneration of muscle has been described by Zenker, and is closely allied to the hyaline degeneration, which he also describes.

(5) **Myxomatous degeneration,** also known as **mucoid degeneration** or **myxomatous metamorphosis.** Myxoma-

tous material is normally found in Wharton's jelly and in the vitreous humor. It is intimately associated with the connective tissues, and arises from the transformation of the cell into a jelly-like substance containing mucin. Chemically, the material seems to be made up of complex albuminous compounds in which mucin is abundantly present; the material is precipitated by alcohol and acetic acid. The affected area is gelatinous and trembling, almost perfectly clear, and colorless.

Microscopically, mucoid material is homogeneous, and not uncommonly contains large multipolar cells with long, branching filaments. These form the matrix which supports the gelatinous material and maintains its conformation; it is not arranged in concentric masses like colloid material.

Myxedema, or *cachexia strumipriva*, is a widespread myxomatous degeneration of the subcutaneous connective and fatty tissues. This peculiar disease is usually associated with, or follows, disease of the thyroid gland; injury to the thyroid and thyroidectomy are not uncommonly followed by the development of myxedema.

Mucoid degeneration occurs in connective tissues, less commonly in epithelial tissues; it occurs in connective-tissue tumors, most commonly in the lipoma, occasionally in sarcoma or chondroma, and rarely in carcinoma.

(6) **Hyaline degeneration,** also known as **vitreous** or **glassy degeneration** or **hyaline metamorphosis.** The exact nature of the material produced, and the method by which it is elaborated, have not been worked out; the body seems closely related to colloid material, but is firmer, more fragile, and arises in a different class of tissues; it is most commonly found in the lymphatic glands, the muscle fiber,—as in typhoid fever,—and blood-vessels and capillaries, around which it may form a distinct mantle; it is occasionally observed just outside the intima of the blood-vessels and around the capillaries, thus closely resembling amyloid material. It does not,

however, give the amyloid reaction. Hyaline material is occasionally observed in the brain, in the stroma of epithelial tumors, and in the dendritic filaments of papilloma of the bladder and other mucous surfaces. Thoma, von Recklinghausen, and Graham look upon hyaline, colloid, mucoid, and amyloid degenerative changes as stages in the life history of one body, the chemistry, pathology, and physiology of which they still consider as unsettled. Zenker, Voight, and Hamilton maintain the above processes to be, for the most part, at least, distinct.

QUESTIONS.

(1) What is an infiltration? (2) Name the infiltrations. (3) Give causes, sites, macroscopic and microscopic appearances of fatty infiltration. (4) Give synonyms of amyloid infiltration. (5) Why is it sometimes called a degeneration? (6) Give causes of amyloid disease. (7) In what organs and tissues is it most common? (8) Describe the appearance of an amyloid organ. (9) Give the chemic tests for amyloid material. (10) What are the sources of pigments in pigmentary infiltrations? (11) Give sources and forms of pigment and methods of infiltration in pneumonokoniosis. (12) What is pseudomelanosis? (13) What is meant by hematogenous pigmentation? (14) What is the difference between hematoidin and hemosiderin? (15) What is a hemochromatosis? (16) What is the source of pigment in jaundice? (17) Of what forms of pigmentation is argyria a type? (18) What is meant by bacterial pigmentation? and give example. (19) What is calcareous infiltration? (20) Give causes and seat. (21) What is glycogenic infiltration? (22) Where is it most commonly found, and what are the chemic tests for it? (23) How would you differentiate glycogenic infiltration from amyloid infiltration? (24) What is meant by degeneration, and how do degenerations differ from infiltrations? (25) Give synonyms of cloudy swelling. (26) Describe the change. (27) Give causes of cloudy swelling. (28) What is the appearance of an organ showing granular degeneration? (29) Give causes, morbid anatomy, morbid histology, and name the most common sites in which fatty degeneration occurs. (30) Give chemic tests for differentiating granular from fatty degeneration. (31) What is hydropic degeneration; give synonyms, causes, and sites. (32) Give same for colloid degeneration. (33) Give microscopic and chemic characteristics of myxomatous material. (34) What is myxedema? (35) Give sites of myxomatous degeneration. (36) What is hyaline degeneration, and under what conditions does it occur, and where is it usually found?

CHAPTER III.

NECROSES.

Necrosis is the local death of a part, as distinguished from somatic death. When necrosis of tissue results from trauma, applied directly to the tissue, it is known as **direct necrosis;** when the change is dependent upon causes applied through the circulation, innervation, or degenerative processes, it is called **indirect necrosis.**

Causes.—Anything which destroys the vitality, *e. g.*, injury, burns, scalds, and chemic destruction. Obstruction to the circulation, whether arrest of the arterial flow to the part or of the venous exit; lymphatic obstruction may have practically the same effect; capillary stasis, thrombosis, or rhexis.

As nutrition is, in part, governed by the trophic nerves, it is held that certain necrotic changes result from lesions of these nerves or the central nervous system acting through them. Such necrotic processes are known as **neuropathic necroses.**

The cause of the necrosis may be complex, more than one element, and in some instances many elements, entering into its formation. In the weak and debilitated, after fevers, in malignant diseases, and, in certain instances, profound shock; necrotic changes are induced by injuries and other causes, which, in the physically strong, would give rise to but little or even no alteration in tissue. As examples of necrosis arising in part through such influences, we have **marasmic** and **senile necroses.**

Results.—The tissue involved may undergo (1) regeneration; (2) absorption, more or less complete; (3) retention, or (4) it may be discharged.

(1) *Regeneration.*—In some instances the necrosed elements are thrown off or absorbed, and adjacent cells, or embryonic constituents of the tissues involved, may produce new tissue identical with that lost, in which case the lost structures are said to be regenerated.

(2) *Absorption* is only possible where the liquefaction can be complete and where bacteria do not gain access; such absorption is typified in bruises where the extruded blood-cells are completely removed.

(3) *Retention.*—The entire mass may be retained, or partial absorption and reparative changes may leave but a part; thus, if an infarct cut off the blood-supply in a branch of the renal artery, the area involved, say a part of a pyramid, dies; after certain degenerative processes, leukocytes and fixed connective-tissue cells wander in and convert the mass into embryonic tissue, from which granulation tissue is evolved and eventually cicatricial tissue (organization). Only a part of the involved tissue may be retained, and this may be much altered, *e. g.*, in the blood cyst or hematoma a fibrous capsule may be formed surrounding the escaped blood. Some of the fluid contents may be removed by the absorbents, and the remaining solid material, consisting of the clot and cellular elements, becomes permanent, or degenerative changes may convert the mass into a cyst.

(4) *Discharge.*—The necrotic mass may be thrown off, as in gangrene, or it may be slowly disintegrated, as in suppuration, ulceration, or caries.

Forms of Necrosis.—Liquefaction necrosis, coagulation necrosis, cheesy necrosis, sphacelation *en masse*, or gangrene.

(1) **Liquefaction necrosis** arises as the result of infection, particularly by pyogenic organisms and irritants which are not sufficiently active to produce coagulation necrosis. It differs from coagulation necrosis in the absence of coagulation; there is the same infiltration of the tissues with fluid, but coagula-

tion does not occur. Pus production resulting from infection represents a type of liquefaction necrosis, in that bacterial products liquefy the intercellular substance which holds the embryonic cells, and thus converts the area involved into a liquid. Liquefaction necrosis is sometimes seen to follow coagulation necrosis, as in blood extravasation.

Site.—White softening of the brain, fluid exudate in burns and vesicles, etc.

(2) **Coagulation necrosis** occurs as the result of infection; as a result of embolism or capillary plugging; in areas of interstitial hemorrhage and in blood-clots, the mass undergoes coagulation necrosis. The tissues are matted together with fibrin, which entangles whatever cellular elements may be present. When occurring in superficial structures, as on or in the mucosa in diphtheria, the fibrin found may be hyaline or homogeneous, fibrillar, and in some instances granular. The view at one time held, that fibrin of the blood was essential to the process, is now admitted to be incorrect, as lymph containing fibrinogen may induce the change. Zenker's degeneration of muscle is, by some, held to be a form of coagulation necrosis. As an example of coagulation necrosis following infection, we have it occurring in diphtheria, tuberculosis, typhoid fever, and allied conditions. It does not seem that bacteria at the point of necrosis are necessary, but that the process may be engendered by the activity of bacterial products; that it is due to the chemic agents is shown by the intravascular injection of *abrin* or *ricin*, which is followed by coagulation necrosis in various organs. After the tissues are matted together by fibrin, fragmentation of the nuclei and more or less complete dissolution of the cell occurs; this may be absorbed, or may undergo the changes already considered.

Site.—Wherever embolism may occur, and in all forms of capillary stasis, it occurs on epithelial surfaces and in glands made up largely of epithelium, such as the liver; the same

condition has been observed in the connective tissues, muscles, and fat.

(3) **Fat Necrosis.**—Whether this deserves a distinct position among the necroses is not fully determined. It is most constantly associated with hemorrhagic pancreatitis, in which condition it occurs in the pancreas, peripancreatic fat, and in the fat of the abdominal wall. It has been found in other conditions, and with no discoverable lesion of the pancreas. The areas of fat necrosis vary in size from one or two mm. to five cm., are usually spheroid or ovoid in outline, are white, and resemble, in a way, disseminated neoplasms or tubercles. In time they may be infiltrated by lime salts; this infiltration is further explained if we accept the statement of Langerhans that the necrotic areas consist of a combination of the fatty acids with lime salts.

(4) **Cheesy necrosis** or **caseation** frequently begins as a coagulation or liquefaction necrosis, followed by a fatty degeneration of the cellular elements and the conversion of the mass into a liquid or semi-fluid material. The fluid is taken up by the lymphatics, in some cases giving rise to *dry caseation* such as is seen in old tubercular abscesses in which the fluid has been absorbed, leaving nothing but the cellular detritus.

Causes.—The process arises almost exclusively in connection with tuberculosis, but is occasionally seen in other chronic infections; in some instances small non-tubercular abscesses may caseate. Caseation is sometimes seen in serous cavities, *e. g.*, pericardium or pleura; rarely, the retention of mucoid materials, as in the Fallopian tubes, may be followed by inspissation and caseation.

Results.—Once the caseous mass is thoroughly capsulated, it becomes permanent; the capsule is likely to become calcareous, and lime salts may be infiltrated into the cheesy material, converting it into a stone-like structure. The con-

dition can not be properly said to be a cure, but only a quiescent stage, likely at any time to be followed by recrudescence of the original exciting cause.

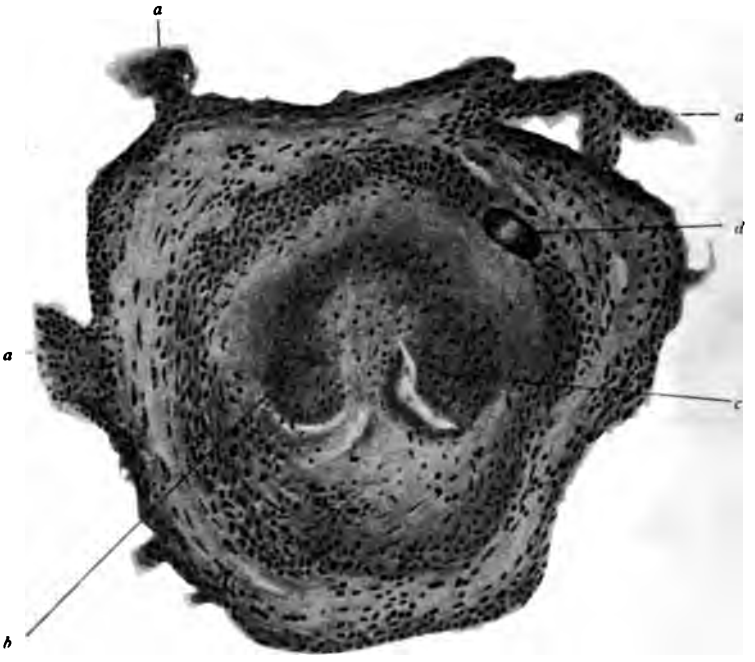


FIG. 101.—CONFLUENCE OF TWO TUBERCLES. SECTION OF LUNG.

Hardened in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. The mass has originated in the vesicular wall, parts of which can be seen at *a*, *a*, *a*, running off to surround adjacent air vesicles; *b* and *c* have been two distinct tubercles, which are now beginning to show caseation. Around the caseous area is a zone of lymphoid cells in which, at *d*, is a solitary giant-cell. Such eccentrically placed giant cells are not frequent. The vesicular walls which leave the tubercle mass at *a*, *a*, *a*, show considerable thickening. (⅛-inch objective, ½-inch ocular.)

(5) **Sphacelation en masse** or **Gangrene.**—This process is also known as *mortification*. A surgical term, *necrosis*, is applied to death of bone *en masse*. Gangrene or mortification is the death of any tissue followed by putrefaction, while attached to the living body.

Varieties.—(*a*) *Moist gangrene*, which is further divided into (1) *circumscribed* and (2) *spreading*; (*b*) *dry gangrene*; (*c*) *hospital gangrene.*

(*a*) **Moist gangrene** may arise from disturbance of the blood supply—arrest of arterial influx, capillary flow, or venous exit. Gangrene may arise from edema; when due to injury, it is known as *traumatic gangrene*; when caused by inflammation, it is called inflammatory gangrene. The inflammatory processes arresting capillary circulation, coagulation necrosis occurs, followed by gangrene. The cutting off of the blood supply may result from occlusion of the artery by an embolus or thrombus, or a similar obstruction of a vein. Continuous pressure upon an area, by progressive lessening of the blood supply leads to softening, and is followed by infection giving rise to gangrene. Destruction of tissue vitality by injury, whether traumatic, chemic, or thermic, leads to gangrene, if putrefaction occur.

Gangrene, in all its forms, represents death of the tissue involved plus infection. Without infection, mummification or drying without putrefaction, would occur. Such a condition is rarely, if ever, seen. The odor of dry gangrene is significant of infection. In *spreading gangrene* a violent infection occurs, spreading by the lymphatics, and with such rapidity as to preclude arrest by the resources of the tissues involved. The infectious processes associated with gangrene are far from worked out. There is, however, a form of spreading gangrene, **malignant edema**, due to a bacillus, which has been thoroughly studied. (See chap. VIII, "Bacteriology.")

Noma is by some considered as a form of gangrene. **Symmetric gangrene**—Raynaud's disease, or **digiti mortui**—is a form of gangrene assumed to be due to arteriovascular spasm. It most commonly involves the same fingers on both hands, and is associated with, or preceded by, nervous or

neuralgic phenomena which indicate its association with the nerves,—sensory and, probably, trophic.

Morbid Anatomy of Gangrene.—The tissues involved become soft, pulp-like, with liquefaction of the fat and cellular elements; as this proceeds, blebs form upon the surface and discoloration occurs, reddish-purple, then black, with varying shades of green. Putrefactive bacteria gain ingress and give rise to the chemic phenomena of putrefaction. Gases may be produced, and these, infiltrating the gangrenous tissue, give rise to *gangrenous emphysema;* the blood pigment breaks down and discolors the fluids, which may be extruded through the skin. The gases of putrefaction give the horribly fetid odor. Where the gangrenous mass joins the living tissue, a line of demarcation occurs; this line represents the point at which the tissue is viable, and where tissue death and the processes of infection are arrested, although the chemic agents engendered below this point may be absorbed. At this line of demarcation embryonic tissue, followed by granulation tissue, develops; these, progressing from the surface, separate the dead from the living tissues; in the soft parts this progresses with considerable rapidity, while in bone the process is much slower. In the dead tissue putrefaction goes on exactly as it would if the tissue was separate from the body; advanced fatty changes occur in the cells, which eventually liquefy. The gases produced are compounds of hydrogen, sulphur, ammonium, etc.

During the destructive metabolism of tissue, induced and carried on by bacteria, in addition to the products already mentioned are certain chemic bodies always the essential result of microbic growth—ptomains. These, for the most part, are highly diffusible, and are rapidly absorbed by the living tissues, and, entering the circulation, give rise to the systemic symptoms of gangrene. As well known clinically, we can understand, pathologically, how the intensity of the symptoms

depend upon the amount of poison generated in the gangrenous focus, the rapidity of its absorption, and the resistance of the patient.

In *spreading gangrene*, the infection promises to be rapidly fatal by its quick spread and the extreme activity of the noxious agents absorbed; hence, the surgeon lays great stress upon the necessity of immediate removal of the invading element. The urgency of the case is augmented by the fact that no line of demarcation occurs.

(*b*) **Dry gangrene** differs from the preceding in that the less juicy nature of the tissues involved resists infection and shows a more marked tendency to mummification. It results from atheroma or obliterative changes in the blood-vessels to the part, and has, therefore, the skin being unbroken, less tendency to a general infection and putrefaction. It is associated occasionally with diabetes and other adynamic states in elderly people having the vascular lesions already noted. It is spoken of as *senile gangrene* and as *diabetic gangrene* under the conditions just noted.

(*c*) **Hospital gangrene** is now a historic disease, modern antisepsis having led to its disappearance. It probably represented an infection, the exact nature of which we can only surmise.

QUESTIONS.

(1) What is necrosis? (2) What is meant by (*a*) direct necrosis, (*b*) indirect necrosis? (3) Give causes of necrosis. (4) What changes may a necrotic area undergo? (5) Name the forms of necrosis. (6) What is liquefaction necrosis, where does it occur, and how does it differ from coagulation necrosis? (7) What is fat necrosis, and where does it occur? (8) Give causes, site, morbid anatomy, and morbid histology of coagulation necrosis. (9) Describe caseation and give causes. (10) What changes may a caseous area undergo? (11) Give synonyms for gangrene. (12) Give forms of gangrene and causes. (13) What is malignant edema? (14) What is noma? (15) What is digiti mortui? (16) What changes occur in gangrenous tissues? (17) Why is spreading gangrene so dangerous? (18) How does dry gangrene differ from moist gangrene?

CHAPTER IV.

CIRCULATORY DISTURBANCES.

Anemia.—The term anemia is used to designate certain changes in the blood in which its functional activity is lessened; but as here considered, reference is made to the **local anemia** dependent upon changes in the circulatory apparatus, and not, essentially, upon changes in the blood itself; it is, therefore, an **ischemia.**

Causes.—(1) Faulty distribution of the blood, as in shock, when the blood tends to accumulate in the larger veins. (2) A very much weakened circulation, whether due to shock, disease, or the influence of poisons, may be too feeble to force the blood through the capillary system, particularly in the skin and brain; hence, cerebral anemia and cutaneous anemia may arise. (3) Diseases of the blood-vessels, such as atheroma; obliterating inflammations of an artery will lead to lessened blood supply in the distribution of that vessel. (4) Pressure. (5) Occlusion of an artery, whether complete or partial, as by ligature, thrombosis, or embolism. (6) Spasm of the blood-vessel due to contraction of its muscular fibers, either dependent upon, or independent of, the innervation.

Morbid Anatomy.—The area is pale and bloodless, and the temperature is likely to be lower than normal; there may be some edema, and, as will be seen later, the stagnation of regurgitation may be evident.

Effect.—If the ischemia be temporary, there will be but slight interference with function; if the process be slowly developed, a gradual lessening of function will occur, and the area may undergo degenerative, necrotic, or atrophic changes;

the same result may follow a slight anemia which persists. If the local anemia be suddenly developed, and the blood supply is insufficient to maintain nutrition, death of the part may ensue; such a condition may follow ligature of the main artery of a limb.

If the cutting off of the blood supply occur in an artery supplied by a branch which communicates indirectly with the area involved, and the circulation be turned through the branch to supply nourishment in the indirect route indicated, such a process is spoken of as *collateral anastomosis*. With the occlusion of an artery the blood-pressure beyond the obstruction gradually lessens until a point is reached where it is less than the pressure in the veins. Backward distention may now occur, so that an area which at one time showed marked ischemia now becomes an area distended by venous blood. This constitutes *stagnation* of *regurgitation*, and probably ends in infarction. (See "Embolism.")

Ischemia is sometimes said to be *collateral* or *compensatory* when it results from the accumulation of blood elsewhere.

Hyperemia. (*Active hyperemia* or *active congestion* of some authors.)—This condition is dependent upon an increased arterial influx; more blood is sent to the part, more blood admitted to the part; there is increased capillary tension as a result of increased blood sent or admitted to the area.

Causes.—(1) Physiologic, as the hyperemia of the mucous membranes during digestion or of the uterine mucosa during menstruation. (2) In inflammation, hyperemia constitutes the first stage, and usually persists during the activity of the processes. (3) Increased arterial pressure or tension; ordinarily, it is probable that the greater quantity of the blood is in the venous system, but when there is increased cardiac activity, the arterial and arteriocapillary systems become surcharged; examples of this are seen in the flushed face of active exercise and in the apoplexy which follows violent exertion. (4)

Neuroparalytic, as when the stimulus to the vasoconstrictors is withdrawn. (5) *Neurotonic*, as when there is hyperactivity of the vasodilators. Hyperemia is said to be *compensatory* or *collateral* when the blood is forced into one area by reason of its inability to enter another, or as the result of anemia elsewhere; such a condition is observed in the increased amount of blood sent to one lung when the other is solid or compressed.

Morbid Anatomy.—During life there is redness, increased cellular activity, usually a slightly elevated temperature; swelling, discomfort, or even pain are likely to ensue; if the process is physiologic, the functional activity is likely to be increased; in pathologic hyperemia inflammation is likely to occur. Persistent physiologic hyperemia may lead to hypertrophy; similar pathologic hyperemia may lead to some of the degenerative processes already described. Postmortem, the evidence of hyperemia may be wanting as the result of the emptying of the arteriole and capillary. Microscopically, however, there will usually be found capillary rhexis, and, if the process has persisted, degenerative or inflammatory changes may have ensued.

Plethora, also known as **polyemia** and **repletio,** implies an abnormal fullness of the entire vascular apparatus. Several forms have been described, dependent upon the material which is increased in the blood, whether it be an increase in the water, in the albuminous compounds, or in the corpuscular elements.

Thoma speaks of a **plethora vera,** in which the blood present is normal; **hydremic plethora,** as dependent upon an additional quantity of water; again, where the plethora seems to involve the entire vascular system, it is said to be **general plethora;** a localized form is described which is analogous to congestion, but is sometimes spoken of as **vascular plethora.** An overdistention of the lymph-spaces is spoken of as **lymphatic plethora,** a condition closely allied to edema.

Anhydremia.—Where the amount of water in the blood is diminished, as is seen in cholera, a condition arises which is spoken of as anhydremia. The water lost from the blood in anhydremia may not of necessity be removed from the body, but may become simply extravascular; this is assumed to be the case in extensive edema.

The retardation in the circulation which occurs as the result of the withdrawal of the normal blood diluent may give rise to cyanotic color and reduction in cutaneous temperature.

Rhexis.—When, through breaking down of the capillary walls or otherwise, red blood-corpuscles escape into the perivascular tissues, the condition is spoken of as rhexis: It occurs in inflammation, in various systemic infections, such as anthrax, malignant edema, and many other mycoses of the blood.

Congestion, also known as *venous hyperemia.* (*Passive hyperemia* of some authors.)—This condition is due to faulty exit of the blood, and to its accumulation in the capillary system of the area involved. In contrast to hyperemia, in which there is an increased amount of arterial blood, in congestion there is an increased amount of venous blood.

Causes.—Any condition which prevents free venous exit, and which at the same time does not limit arterial ingress: pressure, and constricting bands which compress the easily collapsed veins and not the more rigid arteries; diseases of the veins, such as inflammation and thrombosis; tumors, and pressure from surrounding or adjacent organs or structures; in a feeble circulation congestion is favored by gravity, as in the congested extremities of individuals suffering from valvular heart disease; this congestion, dependent upon feebleness of the circulation, is illustrated in the **hypostatic congestion** of the lungs which accompanies typhoid fever and other adynamic states; here the congestion is favored by gravity, as already noted.

Morbid Anatomy.—This is largely dependent upon the duration of the process and its magnitude. During life the area involved is edematous, swollen, bluish, with a temperature usually lower than normal. The process is likely to terminate in degenerative or atrophic changes in the tissues involved; this is due to the fact that nutrition in any given area is as dependent upon the removal of the products of cell life as it is upon the supply of pabulum. Congestion is likely to persist postmortem and be evident, thereby differing from hyperemia. The form of congestion which develops after the cessation of circulation, known as *suggillation*, must be differentiated from congestion which develops during life. Suggillation is not usually accompanied by edema, and does not show the nutritive changes which accompany antemortem venous stasis. (See p. 20.)

Stasis.—When, as the result of the slowing of the circulation, the obstruction of gravity, inflammation, or of injury, the blood stops circulating in the capillaries of an area, the condition is spoken of as stasis. It is a very common sequence of congestion, occasionally occurs in hyperemia, and is a constant phenomenon in inflammation.

Edema implies abnormal or excessive transudation of the fluid portion of the blood into, or its abnormal retention in, the lymph-spaces. As the large serous cavities are generally conceded to be lymph-spaces, the accumulation of serum such as is seen in the ascites, which may accompany cirrhosis of the liver, belongs truly to the edematous condition.

Causes.—Edema arises as a result of some abnormality in the blood, the blood-pressure, or in the vessel walls. Some are inclined to believe that mere changes in the blood will not produce edema until sufficient time has elapsed for the blood changes to give rise, either directly or indirectly, to changes in the vessel walls. The changes in the vessel walls consist, for the most part, of alterations in the endothelium

of the capillaries. The endothelium may become granular, cloudy, or even partially exfoliated. In such abnormal endothelium, enlargement of the stomata occurs, or even separation of the plates along their line of juncture. It is probable that in all forms of edema which arise from increased blood-pressure, some change in the endothelium is an essential part of the process. Where there is an obstruction to the onward flow of the blood, such as may occur from ligature or occlusion of the principal veins, or where there is backing of the blood, which increases the pressure in the capillaries and leads to such degenerative changes in the endothelium as to permit extravasation of the serum, edema occurs. Similarly, venous congestion, due to inability of the heart to propel the venous blood, may induce the same lesion. Normally, the nutrition of the tissues is maintained by serum passing out from the vessels into the perivascular structures (primitive lymph-spaces) and being removed from the tissues by the lymph stream. It will be seen that any obstruction to the onward flow of the lymph, such as may arise by pressure upon the lymph duct, may give rise to an accumulative edema without the necessity of implying any degenerative change in the blood-vessels.

A form of edema known as **edema ex vacuo** is said to occur where brain tissue or tissue from the spinal cord disappears by any process, and the resulting cavity, or loss of tissue, or shrinking of the organ, must be filled in.

Edema is often named for the cause which gives rise to the lesion in the blood-vessel or blood primarily. Such edema may be known as *toxic*, *infectious*, *cachectic*, *traumatic*, *ischemic*, *inflammatory*, *thermal*, or, in some cases (as where the dilatation of the blood-vessels is dependent upon errors or lesions in innervation), the condition may be spoken of as *trophic edema* or *neuropathic edema*.

Morbid Anatomy.—Edematous tissue is usually pale, pits

on pressure, and, as a result of the deficient circulation of the blood, is lower in temperature than the normal. On incising, serum escapes, and the watery condition of the tissue can be readily seen. By reason of the deficient circulation, the resistance of such tissue is lowered, and this renders it extremely susceptible to infectious and necrotic processes. Not uncommonly the edematous tissue shows well-marked and advanced degenerative changes. (See "Hydropic Degeneration," p. 123.)

Ecchymosis differs from any of the preceding conditions in that it represents a hemorrhage into the connective tissue of the part. It is due to injury, and is usually manifested during life, although it may not be recognizable until after death; it very rapidly ensues after the occurrence of injury, and first appears as a blue, livid, or violet color, which gradually changes, after several days, into black, green, blue, or yellow, due to chemic alterations in the blood-coloring matter.

A **petechia** is a small, round, oval or slightly irregular area of ecchymosis due to changes in the blood or blood-vessels; such points occur in scurvy and certain blood-diseases, and can be differentiated from ecchymoses due to injury by the fact that petechiæ occur on the mucous membranes as well as in skin, and are usually in both seats in any given case. Their distinct punctate character renders recognition easy.

THROMBOSIS.

A **thrombus** is an antemortem, intravascular clot. In most instances there is little difficulty in differentiating thrombi from postmortem clots. Coagula formed after death have certain points which are highly characteristic; they are usually smooth on the surfaces, and show no attachment to the vessels in which they lie, although they may be entangled; as, for example, in the muscular columns or the tendinous cords in the heart. This absence of attachment is highly important, even where a thrombus has been dislodged

from its point of attachment. The point will usually be easily recognized as a roughened area upon the blood-vessel wall, the heart cavity, or valves. The postmortem clot has a moist, glistening surface, is usually red in color, always some part of it shows the redness due to red blood-cells, and an important differentiation, for which we are indebted to Cohnheim, is, that in the thrombus there is little difficulty in longitudinal splitting. The thrombus usually has a frayed-out end; a postmortem clot does not show the changes which may be seen proceeding in a thrombus.

Occasionally, where coagulation of the blood postmortem goes on very slowly, sufficient time elapses for the red blood-cells to settle to the most dependent portion, giving a clot the upper layers of which are colorless and jelly-like, while the lower portion shows a deeper color than usual by reason of its containing more red blood-cells.

Very often, when life is almost extinct (agonal period), the very slow rate at which blood may be flowing may give rise to thrombi which become continuous with postmortem clots; coagulation goes on around the thrombus after death. While not restricted to the right side of the heart and the pulmonary artery, such clots are most common in that location.

Red thrombi contain blood-coloring matter usually in the entangled red blood-cells; these are the thrombi which form in stagnant blood. **White thrombi** are thrombi consisting of fibrin with a varying number of leukocytes, and occur in flowing blood. Thrombi may be mixed, the so-called **gray thrombi,** in which the gradual slowing of the blood has led to a slight deposition of the red blood-cells with the fibrin. Where the thrombus is made up of layers, such as occur in the cavity of an aneurysm, the thrombus is said to be **stratified.** When a thrombus remains where it originated, and arises independent of other thrombi, it is spoken of as a **primary thrombus.** The term **propagated thrombus** is applied to

a thrombus which extends some distance from the point at which it originated; such thrombi are extremely likely to show different ages at different points, and may extend to an indefinite length. A thrombus developing from an embolus, or a thrombus which arises secondary to an existing thrombus, is spoken of as a **secondary thrombus.** When a thrombus leads to occlusion of the blood-vessel in which it lies, it is said to be an **obstructing thrombus.** When it permits of the blood floating one way and would occlude a current in the opposite direction, it is spoken of as a **valve thrombus.** Where the thrombus lines the wall of the cavity, *e. g.*, an aneurysm or a blood-vessel, it is said to be a **parietal** or a **mural thrombus.** When a thrombus extends around a blood-vessel, it is said to be **annular.** Where a thrombus has formed with a distinct canal, it is spoken of as a **channeled** or **canalized thrombus.** The "*ball thrombus*" and *floating thrombus* are rarely attached; examples of these are seen in the cardiac ventricles or auricles, and occasionally in aneurysm. The most important division of thrombi is into **simple** and **infected** or **infective,** the former meaning aseptic thrombi, containing no bacteria, the second meaning thrombi containing bacteria, hence *infected thrombi.*

Thrombi are sometimes spoken of as **arterial** or **venous,** and, under the latter, a separate form is named dependent upon its location in a distinct venous system—**portal thrombi.**

Causes.—The essential exciting cause of the thrombus is that process which terminates in coagulation of the blood. Other causes are: (1) Any body within the circulation, not covered by endothelium, will lead to attachment of the third corpuscle and the subsequent formation of a clot or thrombus; (2) roughening of the vascular wall, as observed in atheroma; (3) slowing of the circulation as occurs in partial occlusion of a blood-vessel, or in complete occlusion, as represented by ligature. It is maintained,

and probably justly, that a blood-vessel may be ligated and its lumen occluded without intervention of any clot. This implies great care in applying a ligature so that it does not injure the endothelium. It is not probable that a ligature is ever so applied. When a blood-vessel is ligated in its continuity, a thrombus forms on the cardiac side which is known as the **proximal thrombus,** and the thrombus formed in the blood-vessel beyond the ligature is known as the **distal thrombus.** It is probable that complete or partial obstruction gives rise to changes in the endothelium of the vessel wall, and this favors the mural lodgment of leukocytes and third corpuscles, and hence a thrombus. (4) Any alteration in the vessel wall which injures the endothelium favors the development of a thrombus. (5) Chemic changes in the blood also favor the development of thrombi; examples of these are seen in diphtheria and in adynamic conditions with very much slowed and enfeebled circulation. Such thrombi are spoken of as **marasmic thrombi.** (6) Hyperinosis, such as develops in pregnancy, is nature's method for anticipating hemorrhage, the increased amount of fibrin favoring the arrest of bleeding by the development of thrombi. (7) Chemic changes leading to a thrombus may be produced in the blood by the injection of certain agents, *e. g.*, ether. (8) Where a tumor infiltrates or comes in contact with a blood-vessel, a thrombus is likely to form. (9) A primary thrombus favors the development of secondary thrombi. (10) Mycoses of the blood favor the development of thrombi. (11) Embolism favors thrombus formation.

Changes Which a Thrombus May Undergo.—These changes are dependent upon whether a thrombus is *simple* or *infective.* In **infective thrombi** the only changes which are likely to occur are those phenomena constantly associated with infection, namely, *liquefaction, softening,* or *breaking down;* rarely, in infected thrombi, dislodgment may occur. The changes to

be considered in *simple thrombi* almost never occur in the infected thrombi, with the exception of softening. The fragments of an infected thrombus become infected emboli, and

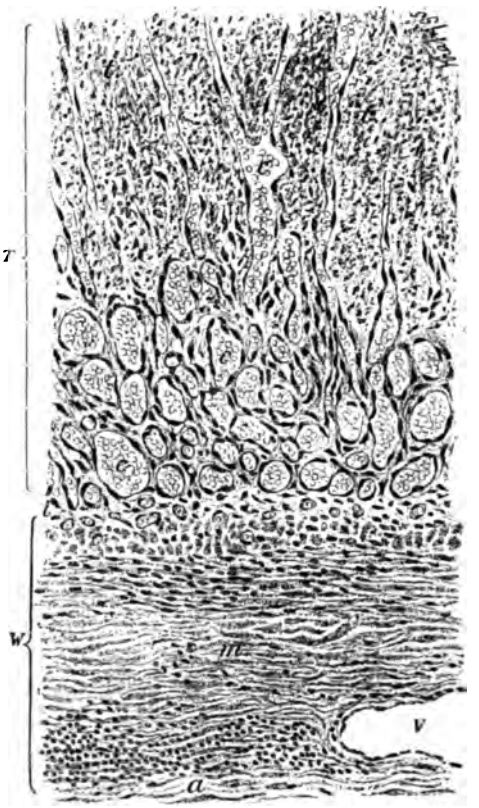


FIG. 102.—SECTION THROUGH A PART OF A VEIN WITH ITS CONTAINED ORGANIZING THROMBUS.—(*Schmaus.*)

W. Wall of vein. *a.* Adventitia. *m.* Media. *i.* Intima. *V.* Blood-vessel in the wall of the vein. *T.* Thrombus now largely composed of granulation tissue. *c.* Young blood-vessels; those near the intima are larger and more fully developed than those extending into the thrombus, the latter being younger.

lead to the dissemination of the infective material and its deposition in other parts of the organism; besides this, infected

thrombi are constantly throwing into the circulation bacteria or the products of bacterial life, this condition constituting what is known as *septicemia* or *mycosis* of the blood. Where the infective material contains the organisms of suppuration, and the emboli, lodging, give rise to abscesses, such abscesses are spoken of as *pyemic* or *metastatic*, and the disease is known as *pyemia*.

The changes which may occur in simple, non-infected thrombi are *dislodgment*, *decolorization*, *re-solution*, *softening*, *organization*, and *calcification*.

(1) *Dislodgment.*—This occurs but rarely. The cases which I have observed have been from large tumors of the uterus, where a thrombus has formed in one of the massive sinuses of such a tumor, and, becoming dislodged, has reached the lung and blocked the larger vessels to that organ, leading to almost instant death.

(2) *Decolorization.*—Decolorization is possible only in the red thrombus, and is due to the gradual absorption of the coloring matter by the circulating blood which flows over, around or through it.

(3) *Re-solution.*—It is hard to demonstrate when this process occurs; but there can be no doubt that the simple, non-infected thrombus, due to temporary conditions, may be dissolved, or may undergo solution upon the removal of the cause.

(4) *Softening.*—This is not so common in the simple as in the infected thrombus, and is usually due to conditions of development and to blood changes which militate against the process of organization. When softening and breaking down occur, the fragments, reaching the circulation, form *simple emboli;* more commonly, instead of softening, there is really a condition of *fragmentation* in which merely the end of a thrombus is broken off.

(5) *Organization.*—In the study of organization we have but to consider the method by which a blood-vessel heals.

There is developed within the blood-vessel a thrombus; a clot or fibrinous exudate forms around the point of ligature external to the vessel; leukocytes and fixed connective-tissue cells of the blood-vessel, represented by its endothelial lining, proliferate; as a product of this we have embryonic tissue; from the vasa vasorum we have capillaries developing into this mass, converting it into granulation tissue, and eventually into cicatricial tissue. This thrombus and the cicatrization extends

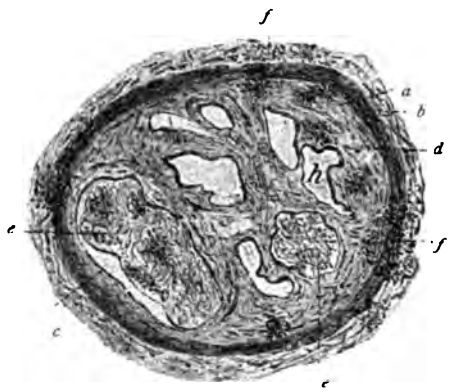


FIG. 103.—TRANSVERSE SECTION OF A THROMBOSED BLOOD-VESSEL IN WHICH ORGANIZATION AND CANALIZATION OF THE THROMBUS ARE IN PROGRESS.

a. Newly formed connective tissue of the thrombus. *b*. Tunica media. *c*. Tunica intima. *d*. Young cell infiltrate of the thrombus. A similar infiltrate of the coats of the vessel is shown at *f*, *f*. *e*. Remainder of the not yet organized thrombus. *h*. Developing canals.

back to the first collateral branch which is carrying on its circulation. Wherever a thrombus organizes, the changes developed are analogous to those studied in the repair of a blood-vessel.

(6) *Calcification.*—Where a thrombus forms in a slowed circulation, *e. g.*, of a dilated vein, and is attached to the vein or lodged in the sinus of the valve, infiltration by lime salts not uncommonly occurs and produces the so-called *phleboliths* or "*vein-stones*"; infiltration of lime salts is also likely to

occur in the thrombus which is organizing or which has organized.

Modifications of some of the above conditions are occasionally considered as separate processes; thus a large thrombus may undergo a *central softening* and postmortem, or during an operation—*e. g.*, on aneurysm—a thrombus may be found in which fatty degeneration or liquefaction necrosis has occurred in its center, which will be found filled with the reddish or yellowish fluid; this was at one time spoken of as cystic degeneration of a thrombus. An attached thrombus may remain more or less quiescent for a considerable length of time, or the changes which it may undergo may be so poorly marked as to be scarcely recognizable.

Results of Thrombosis.—These are largely dependent upon the character of the thrombus and upon the changes which the thrombus itself has undergone; the results due to such changes will suggest themselves, *e. g.*, an organizing or obstructing thrombus may more or less occlude the blood-vessel; the evidence of such occlusion will be dependent upon whether the blood-vessel is the main trunk to a limb or one of the less important branches; again, if the thrombus form slowly, the collateral circulation may sustain the nutrition to the limb or part. The alterations produced in the blood-vessel are dependent upon the changes which the thrombus undergoes; these also suggest themselves.

EMBOLISM.

An **embolus** is any solid substance thrown into the circulation. As Park states, the essential element is transportation or carriage of some solid or semi-solid body in the circulation. Emboli are usually too large to pass the capillaries. They may be composed of (1) thrombi detached or in fragments; (2) fragments of the cardiac valves or vegetation from the valves; (3) calcareous plaques; (4) fragments of tumors;

(5) purely extraneous bodies, such as pieces of bone, or oil globules which may gain ingress by fracture or injury to bone, and air; (6) certain parasites, such as the echinococcus. The most important classification of emboli is the division into **simple** and **infective,** the terms having the same meaning as already given when considering thrombi.

Changes Induced by an Embolus.—An embolus floats along in the blood stream until it reaches the bifurcation of a blood-vessel either branch of which is too small to transmit the mass. It then lodges, obstructs the stream, and gives rise to a thrombus; the blood supply transmitted by the vessel involved is arrested. In certain parts of the body the blood-vessels are more or less *terminal;* any given area is supplied by a single branch, and this branch receives but little, if any, blood from collateral branches. Terminal arteries are found in the brain, spleen, and in the kidney. With the lodgment of an embolus the blood-vessel beyond the point of lodgment empties itself, and the area becomes anemic; refilling of the vascular area occurs from the vein, and we have produced a condition known as **hemorrhagic infarction.** The area is now swollen, it is more or less conic in shape, as the result of the shape of the area in which the vessel involved is distributed. Where the blood-vessel is not terminal, the shape of the area involved is dependent entirely upon the extent of the collateral circulation. However small or large the area, the changes within it are dependent upon the character of the embolus which produced it, whether simple or infective. The infarcted area of a simple embolus undergoes the following changes: (1) There is coagulation necrosis in which all of the tissues involved are matted together by fibrin; the area is now firm, swollen, red or brownish, and, if it reach the surface of the organ, is elevated. (2) If the area be very large, as a result of cutting off of the blood supply, the center may undergo fatty degeneration and soften, converting it into

a cyst; where this liquefaction necrosis has occurred, the fluid produced may be absorbed and cicatrization may ensue, or the fluid may remain as a cyst. Where the area is smaller, we have repair occurring by the proliferation of the connective-tissue elements and of the leukocytes, the production of embryonic tissue and cicatrization; into this lime salts may be infiltrated. (3) By reason of the reduced resistance of the tissue as a result of the nutritional changes incident to the lodgment of an embolus, we may have an area, in which the original infarct was simple, become infective, or what is more commonly correct, become infected.

In the area of infarction due to the lodgment of an embolus containing infective material, we have engendered whatever process may arise as the result of the specific agent which the embolus contains; thus, if the organisms of suppuration be present, an abscess is formed known as a *metastatic abscess*, or *embolic abscess;* by reason of the constant presence of these abscesses in pyemia they have long been known as pyemic abscesses. If the embolus contain tubercle bacilli, tuberculosis will result; if the embolus contain the specific cells of the tumor, *e. g.*, a sarcoma, we have developed a secondary tumor; beside all this, infected emboli give rise to secondary thrombi, and these are liable to undergo exactly the same changes which the primary thrombus underwent.

Thrombi or emboli are sometimes spoken of as (1) *arterial*, (2) *venous*, or (3) *capillary;* multiple; miliary; traumatic; neoplastic, arising from tumors; specific and non-specific; simple and malignant: these terms explain themselves.

Occasionally an embolus arising in the venous system passes directly from the right to the left side of the heart, through a defect in the septum between the auricles or ventricles, in which case it is spoken of as a **paradoxic** or **crossed embolus.** In very rare instances, as a result of sudden alterations in the blood-pressure affecting only one area, we may

have emboli floating backward in the venous stream, producing what is known as **recurrent embolism**, or they are called **retrograde emboli.** This was, at one time, assumed to explain certain abscesses of the liver, which are now recognized to be due to emboli arising in the portal system. They are very rare.

QUESTIONS.

(1) What is meant by ischemia? (2) Give causes and morbid anatomy. (3) What changes may the ischemic area undergo? (4) What is hyperemia? give causes, forms, and morbid anatomy. (5) What is meant by plethora? (6) What are the forms of plethora? (7) What is rhexis? (8) Give synonyms for congestion, causes, and morbid anatomy. (9) Give causes, morbid anatomy, and tissue changes which occur in edema. (10) What is ecchymosis? (11) What is meant by petechia? (12) What is a thrombus? (13) How differentiate a thrombus from a postmortem clot? (14) Give forms of thrombi. (15) What is the most important division of thrombi? (16) Give causes which induce thrombosis. (17) What is meant by (*a*) proximal thrombus? (*b*) distal thrombus? (18) What changes may a thrombus undergo? (19) How are those changes influenced by the presence or absence of infection? (20) What is an embolus? Give its causes, and the changes which it may induce. (21) What is meant by (*a*) pyemic abscess? (*b*) infarction? and what changes may an area of infarction undergo? (22) What is meant by a crossed embolus and recurrent embolism?

CHAPTER V.

INFLAMMATION, REPAIR, AND REGENERATION.

INFLAMMATION.

Probably the most acceptable definition of inflammation is that given by Park, which is, as he states, a modification of Sutton: "Inflammation is an expression of the effort made by a given organism to rid itself of, or render inert, noxious irritants arising from within or introduced from without." It is probable that inflammation represents the process of repair plus infection or the removal of dead tissue; that these are not the exclusive elements is indicated by the fact that by the injection of certain chemic agents all the phenomena of inflammation may be produced; *e. g.*, the production of suppuration by the infection of tuberculin is one of the most efficient experimental methods. Practically, such conditions do not enter into the causes of inflammation as studied clinically, while the tissue reactions to dead tissue and to infection are the essential elements with which we practically have to deal; the causes given by older writers embrace these elements, *e. g.*, trauma means destroyed or injured cells; chemic causes include destroyed cells; thermic causes embrace dead tissue elements, etc.

Terms Applied to Inflammatory Processes.—Inflammation is said to be *simple* or *common*, a term used in the same sense as applied while considering thrombosis. *Infective* or specific is used in inflammation in the same sense as in thrombosis. With regard to time and the activity of the process, inflammations are said to be *acute*, *subacute*, or *chronic*. In full-blooded individuals, with abundant nutrition, the inflammations are

likely to be *sthenic;* under reverse conditions they are spoken of as *asthenic* or *adynamic*. In regard to the organ or tissue involved, they are spoken of as *parenchymatous* when the functionating cells of the organ are involved; or *interstitial*, where the connective tissue is invaded (*e. g.*, see "Inflammation of the Kidney"). Inflammations of the serous membranes are spoken of as *serous*, *plastic*, *adhesive*, *fibrinous*, *exudative*, etc. (see chap. IV, part III, "Serous Membranes"). *Purulent phlegmonous* or *suppurative* inflammations are properly here classified as infectious. While considering inflammation of mucous membranes, reference will be made to *pseudomembranous* or *croupous*, *diphtheritic* or *gangrenous*, *catarrhal*, and *hemorrhagic* inflammations.

Morbid Anatomy.—The elements to be studied in inflammation are (1) the blood-vessels; (2) the intravascular changes, or the blood; (3) the perivascular changes.

(1) *Changes in the Blood-vessels.*—With the inception of the cause, there is a contraction of the blood-vessels which is very brief, and there is no evidence that it always occurs; immediately following this, the blood-vessels dilate; the dilatation is first regular and then varicose, and eventually saccular, the blood-vessels becoming tortuous and irregular. These changes are probably due to the increased capillary tension and the influence of noxious agents directly upon the vessel wall. The intracapillary tension is probably raised by relaxation of the arterioles through which the blood supply to the part is admitted.

(2) *The Changes in the Blood and Blood Currents.*—The current is primarily accelerated, but with the dilatation of the blood-vessel the current becomes gradually slower; following the slowing there is *oscillation*, and eventually there is *stasis* or *stagnation*. With the slowing of the blood current the corpuscular elements, instead of being equally distributed, arrange themselves in two streams, (*a*) an *axial stream*, occu-

pying the center of the blood-vessel, largely composed of the red blood-corpuscles, and, therefore, spoken of as the *corpuscular stream;* (*b*) the *circumferential* or the *parietal* stream, also called the *plasmatic stream*, which surrounds the axial stream and is composed largely of plasma and leukocytes, with which there are at first a few red blood-corpuscles, but as the leukocytes adhere to the vessel wall, the red corpuscles pass into the axial stream. The leukocytes, as a result of alteration in the vessel wall, and also as a result of their ameboid movement, pass through the vessel wall into the perivascular tissues; at

FIG. 104.—LEUKOCYTES OF A FROG.—(*Stohr.*) × 560 diameters.

Extending out from the side of the leukocyte will be seen a number of projections called pseudopods. In the diapedesis or migration of the leukocyte through a blood-vessel wall in inflammation, these pseudopods are first thrust through the wall, the cytoplasm of the leukocyte flowing through into the pseudopod, carrying with it the nucleus, thereby delivering the cell upon the outer side of a blood-vessel wall.

the same time there is poured out into the perivascular tissues an excess of the liquor sanguinis; these changes relieve the intracapillary pressure, and the circulation may be re-established; if the cause, however, continue to act, the phenomena just described may be repeated. When the stasis or stagnation becomes permanent, the red corpuscles arrange themselves like so many coins piled upon each other (rouleaux); this is followed by fragmentation of the cells and coagulation necrosis. During the stage of increased intracapillary tension, with the capillary walls injured, there is likely to be an escape of red blood-corpuscles; these probably pass through a rupture in

the wall, the process being known as *rhexis;* the amount and number of red corpuscles present in the perivascular tissues is usually in direct proportion to the severity of the inflammation and the character of the tissue; lax tissues, with poorly supported capillary walls, show more infiltration than dense, resisting structures.

(3) *Changes in the Perivascular Tissues.*—The lymph-spaces of the perivascular tissues are crowded by leukocytes and exuded liquor sanguinis; as a result of the increased pabulum supplied, proliferation of the fixed connective-tissue cells and the migrated leukocytes occurs. This cell proliferation terminates in the production of a small round-cell mass, known as *embryonic tissue*, *indifferent tissue*, *inflammatory new formation*, *round-cell infiltration*, etc. The round cells which compose the tissue are held together by an albuminoid, gelatinous, intercellular cement.

Termination of Inflammation.—If the cause of the inflammation be withdrawn prior to the proliferation of the cells in the perivascular tissue, the leukocytes re-enter the blood stream, or, with the liquor sanguinis, pass off through the lymphatics; the disturbed circulation gradually returns to the normal, and the tissue is left without any permanent evidence of the disturbances through which it has passed. After the production of embryonic tissue, the changes which ensue are dependent upon the cause. If due to infection by pyogenic bacteria, these, by their chemic product, liquefy the intercellular substance and liberate the embryonic tissue cells and leukocytes, these constituting the pus-corpuscles; the liquefied intercellular substance, with the liquefaction of any fibrin which may be present, and the infiltration of the area by serum, produces the *liquor puris* or *pus liquor*. The character of the pus is dependent upon the agent which gives rise to the infection and upon the virulence or quantity of the infectious agent present.

Where the pus is retained in the tissue involved, the accumulation constitutes an **abscess.** The wall of the abscess is formed of the tissues involved, to which, however, is added the elements of the surrounding active inflammation. The center is made up of the debris resulting from the battle between the leukocytes and the infectious agents—the bacteria. Surrounding this is a wall composed of breaking-down tissue containing leukocytes, fibrin, embryonic tissue, and the more or less altered normal tissue of the part; from this zone there gradually fades off into the surrounding tissue a zone loaded with leukocytes actively engaged in combat with the bacteria, considerable fibrin, and serum, giving us the edema so constantly seen around an abscess. The line of least nutrition and density is the path of least resistance through which the infection travels until a surface is reached through which the pus is evacuated. The removal of the necrotic tissue, and the overcoming of the infection by the protective agencies of the area, permits of reparation by the production of embryonic tissue into which young blood-vessels are thrown out, converting the embryonic tissue into granulation tissue. The walls of the abscess, collapsed together, repair by the union of the two granulating surfaces, a mass of fibrous tissue marking the site of the abscess.

If the destruction of tissue has been superficial, as on the skin or mucous membrane, the resulting loss of structure constitutes an **ulcer.** There is supplied in the same way embryonic tissue, followed by granulation tissue, which completes healing by the growth over its surface of the epithelium arising from the epithelial borders of the ulcer.

Where the process is not due to infection, with the subsidence or withdrawal of the cause, the removal of dead tissue, or the disappearance of an irritant, repair ensues, and the embryonic tissue becomes vascularized from the nearest blood-vessel and organizes into cicatricial or scar tissue.

Morbid Physiology of Inflammation. — The cardinal symptoms of inflammation are heat, pain, discoloration, swelling, and disordered function.

(1) *Heat* is due to the (*a*) increased vascular activity; more blood flowing through the area—quickened circulation—means more heat carried to the point involved; (*b*) the increased cellular metamorphosis; (*c*) the increased oxidation which is going on in the area involved; (*d*) theoretically, the friction of the increased blood currents and the impact of stasis must increase the temperature, but practically they can be of but little import.

(2) *Pain* is due to pressure or stretching of the nerves by the swelling, and to the irritant influences of the inflammatory exudates upon the nerve filaments.

(3) *Discoloration* is dependent upon the (*a*) increased amount of blood in the area; (*b*) the proliferation of the cellular elements; and (*c*) the character of the inflammatory exudate; thus, the increased amount of blood may give rise to redness, which becomes scarlet, brownish or bluish, passing through the different shades to black. In non-vascular exudates the structure may be white instead of red; this is shown in the cornea, where we have the ground-glass appearance, due to the inflammatory products, there being no red blood-corpuscles in the cornea. The redness is represented by the inflammation of the adjacent conjunctiva. The exudate in inflammations of serous membranes renders the surface white, unless the inflammatory processes be hemorrhagic.

(4) *Swelling* is due to (*a*) the increased amount of blood in the part; (*b*) the proliferation of the cells; (*c*) the exudate in the perivascular tissue.

(5) *Disordered function* is due to (*a*) alteration in the tissue cells present, both the essential functionating cells and the interstitial elements; (*b*) the interference with function resulting from the exudates; and (*c*) the fact that the exudates

prevent the activity of the innervation upon which the function of all tissue so largely depends.

Systemic Phenomena of Inflammation.—These are largely embraced in the term *fever*, and are due to the absorption of the inflammatory materials from the seat of the morbid process. The character of the fever and the severity of its manifestation are dependent upon the activity of the agents absorbed. In the simple aseptic fluids taken up by the lymphatics from an ordinary sterile wound, such as is typified in a broken bone, the manifestations are slight and temporary. When the materials absorbed contain the products of bacterial life, marked alteration in the tissue elements elsewhere in the body may occur. Degenerative processes arise in the viscera independent of the presence of bacteria. The disturbances of glandular activity are represented in the diminished secretions and excretions. The epithelial surfaces show, under the influence of bacterial agents, a decided tendency to undergo degenerative processes; this is most marked the more severe the infection, so that in the gangrenous and specific inflammations—for example, those of diphtheria—coagulation necroses in the large glandular viscera are not uncommon. The nervous phenomena which accompany inflammation are probably due to the direct action of the poison under consideration on the nerve substance, or the influence of the poison upon the capillaries distributed in the nerve tissues, giving rise to inflammatory or degenerative processes in those structures. Exactly what causes the condition called fever will be discussed later (see chap. x).

REPAIR.

Cell Reproduction.—As a part of the processes of repair (repair modified by infection, regeneration, inflammation so-called, hyperplasia, certain forms of hypertrophy, etc.), prolification, proliferation, or reproduction of cells must be studied. There are two methods by which cells reproduce themselves:

(1) *Direct division* or *amitosis*. (2) *Indirect division*, also known as *karyokinesis*, *karyomitosis*, and, quite commonly, as a more convenient term, as *mitosis*.

(1) **Amitotic Division.**—In this form of segmentation the cell shows a constriction which involves both the cell protoplasm and the nucleus. This constriction is followed by a separation of the two portions, the nucleus first dividing and passing to the two ends of the protoplasm, which gradually separates, giving rise to two cells; during the process there is no manifest systematic change in the chromatin of the nucleus, as is seen in the next form.

(2) **Mitosis.**—As a rule, the cell only divides into two parts; this is not, however, constant, as occasionally three cells may be developed simultaneously from one cell (J. Arnold). The steps of mitosis may be approximately stated as follows: In the resting nucleus the chromatin increases and groups itself as a skein, which later becomes thinner (*mother skein*). During this process the nuclear membrane disappears, and, if the cell possessed a nucleolus, this is lost sight of. Immediately following this, probably in progress at the same time, there are soon developed, probably from the achromatin, delicate lines which pass off toward the two poles of the cell, giving the central portion of the cell an arrangement shaped like a spindle, and hence the name *nuclear spindle*. The chromatin now divides transversely to this nuclear spindle, and passes, one-half in each direction, toward the points of the spindle. The mass of the chromatin, at each end of what was the spindle, now constitutes what are spoken of as the "*daughter stars*." During the arrangement of the chromatin as daughter stars, an hour-glass-like contraction of the protoplasm of the cell appears, developed by an annular narrowing gradually developed around the center of the cell. At first the daughter stars situated in the two poles of the cell are joined by delicate striation, which probably represents the remains of the achro-

matin formerly constituting the nuclear spindle; these lines disappear, the two masses of chromatin show now no connection, and the hour-glass contraction is completed, separating the cell into two parts, in each of which parts there is a daughter skein, which now rearranges itself as a resting nucleus around which a new nuclear membrane may appear.

Lavdowsky has described another form of cell division

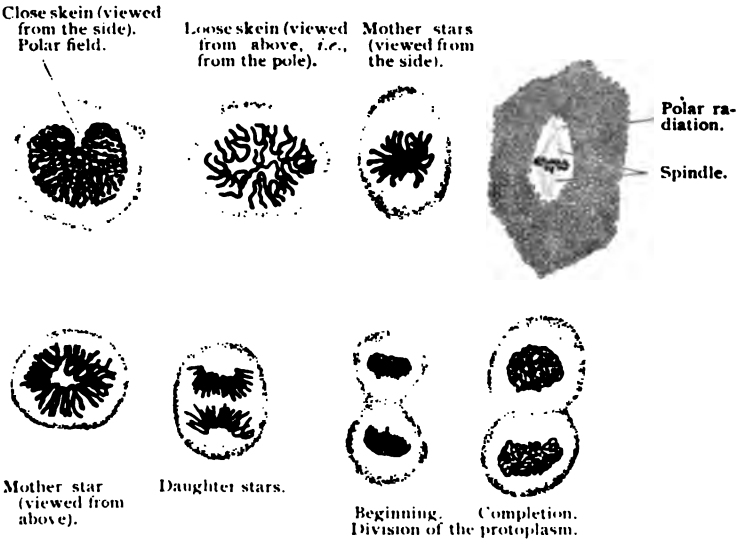

Close skein (viewed from the side). Polar field.
Loose skein (viewed from above, *i.e.*, from the pole).
Mother stars (viewed from the side).
Polar radiation.
Spindle.
Mother star (viewed from above).
Daughter stars.
Beginning. Completion.
Division of the protoplasm.

FIG. 105.—KARYOKINETIC FIGURES OBSERVED IN THE EPITHELIUM OF THE MOUTH CAVITY OF A SALAMANDER.—(*Stohr.*) × 500 diameters.

The picture in the upper right-hand corner is from a section through a dividing egg of Siredon pisciformis. The centrosomata, also the first stages of the development of the spindle, can not be seen by this magnification.

which he calls "*division by force.*" It appears in this form: two portions of the protoplasm of the cell move in opposite directions, apparently pulling themselves apart. Thoma has described and figured this process as occurring in the white blood-cells of the frog when stimulated by electricity.

Inflammation is repair plus the removal of dead tissue or

infection. Where there is no dead tissue to remove, or where this is in a minimum, and where there is no infection, injury to tissue is followed immediately by the process of repair.

As studied by the surgeon, healing is said to occur by (1)

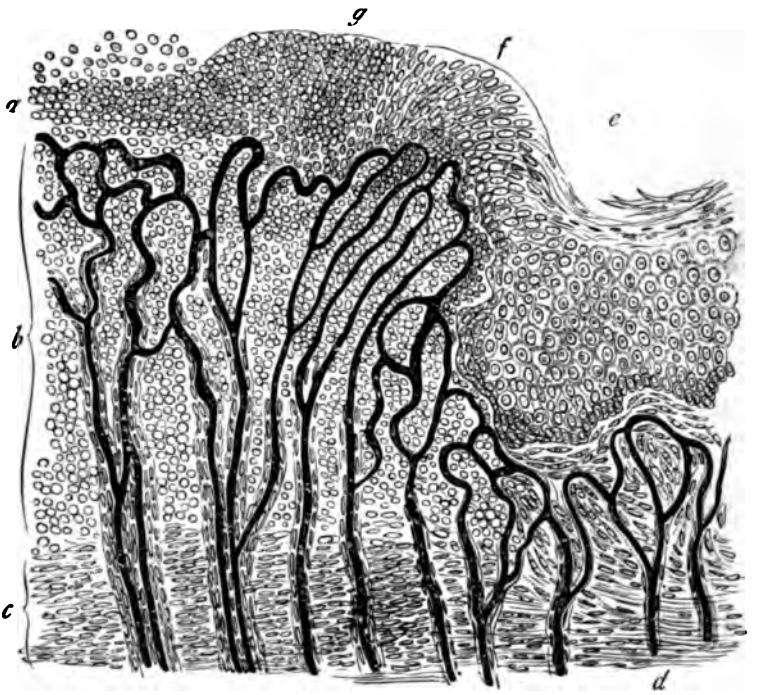


FIG. 106.—SECTION THROUGH THE BORDER OF A HEALING WOUND.—(*Rindfleisch.*) × 300 diameters.

a. Surface of ulcer. *b*. Granulation tissue composed of embryonic tissue with the capillary loops developed from the vessels below. *c*. Later stage in the development of the granulation into spindle-cell elements, young cicatricial tissue which is older at *d*. *e*, *f*, *g*. The epithelium spreading over the surface of the healing area.

first intention. Thus, if the surfaces of a recent wound be brought immediately in contact and retained, the following phenomena occur: Liquor sanguinis is poured out, immediately followed by its coagulation, forming a fibrinous cement—the

so-called inflammatory lymph—which binds the two sides of the wound together. Into this leukocytes wander from the adjacent blood-vessels, and, with the connective-tissue cells from the sides of the wound, proliferate, forming embryonic tissue. Into this young blood-vessels are thrown from the adjacent capillaries, converting the mass into granulation tissue, and this organizes into cicatricial tissue.

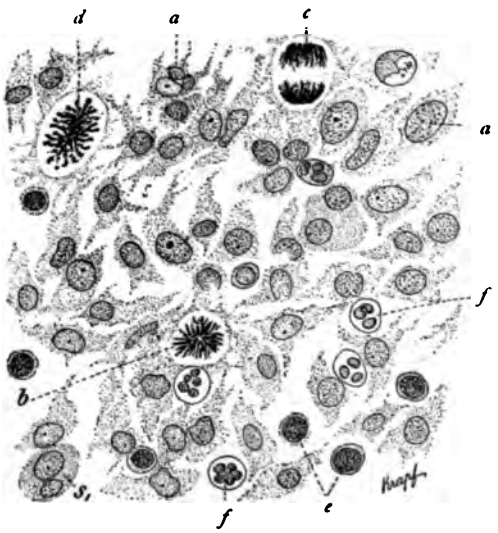


FIG. 107.—CELLULAR ELEMENTS OF GRANULATION TISSUE.—(*Schmaus.*)
× 500 diameters.

a. Spindle-forming, star-forming, and round cells. *b*. Mother star. *c*. Daughter star. *d*. Skein stage. *e*. Round cells. *f*, *f*. Leukocytes (?).

A form of repair which closely resembles repair by first intention, is repair upon a *framework* or "*scaffold*." To illustrate how this may occur, let us suppose that there is a large "dead space," such as would occur after the chiseling away of bone; into this dead space blood oozes and coagulates. The coagulated fibrin forms a scaffold upon which young blood-vessels, embryonic and granulation tissue advance from

the sides and eventually complete the process of repair. In bone, ossification is also produced by the formative bone-cells of the adjacent tissue. This is illustrated also in the repair of fractures, in which the blood thrown out around the end of the bone acts as a "scaffold" upon which the process of repair proceeds. Other materials than blood have been used for the

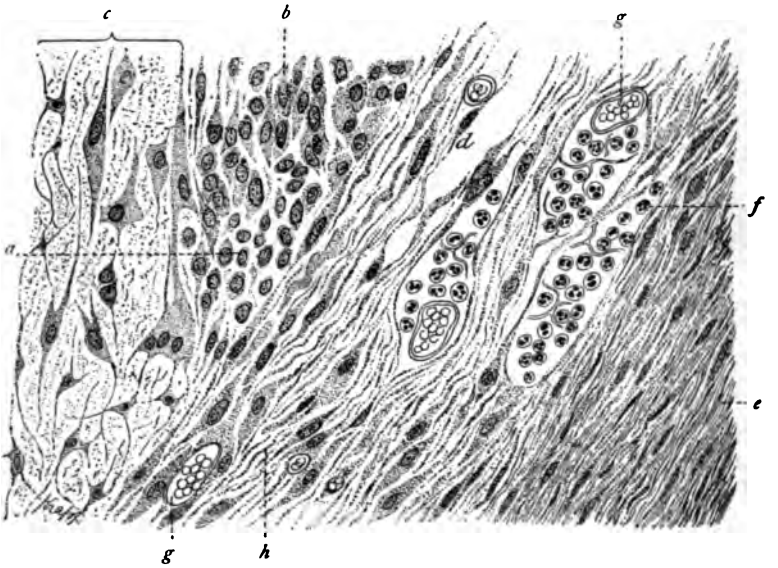


FIG. 108.—GRANULATION TISSUE. LATER STAGE IN ORGANIZATION THAN FIGURE 108. —(*Schmaus.*) × 250 diameters.

a. Round cells. *b*. Forming spindle cells. *c*. Forming spider cells, multipolar cells. *d*. Space from which cellular elements have dropped out; possible primitive lymph-spaces. *e*. Point where the spindle-forming process is advanced. *f*. Leukocytes with severed nuclei (fragmented nuclei). Through this area will be seen young capillaries; the same are shown below the blood-vessel indicated by the upper *g*, *g*, *g*. Blood-vessels. *h*. Matrix of intercellular substance with forming spindle cells.

scaffold; sponge, chips of bone, cartilage, ivory fragments, and allied substances which can be readily antisepticized, may be used.

(2) Healing by **second intention** is said to occur in wounds whose edges can not be brought together, and where

the scaffolding process, already referred to, is not available. The ordinary recent, traumatic ulcer is an illustration of this process. Suppose that considerable skin surface is removed, and a raw surface presented for healing. Within a few hours a layer of coagulated fibrin will be seen upon its surface. Into this the formative cells will wander, producing embryonic tissue. Young capillaries spring out from the adjacent vessels, and convert the embryonic into granulation tissue. By continuous proliferation of the cellular elements, with pushing up of the capillaries, the cavity is gradually filled, and when this new tissue reaches the surface, covering over by epithelium occurs.

The epithelial regeneration is secured from the living layers near the edge which proliferate, and by extension from all directions, in favorable cases, gradually cover the granulating surface. Epithelium may be engrafted upon the embryonic tissue, and new centers of epithelial regeneration be thus established.

Another form of healing, which is truly repair by second intention, is sometimes referred to as healing by **third intention.** This is illustrated when we bring two granulating surfaces together; the two adhere, blood-vessels pass from one to the other, and cicatrization occurs exactly as already described. It was once said that union under a scab represented another form of healing, but it is now recognized that granulation and skinning over by epithelium, as already described, occurs. It is not, therefore, a distinct process, but merely a form or combination of some of the above.

Regeneration.—Repair may occur without regeneration. Thus, muscle may be repaired by fibrous tissue, the scar joining the severed ends of the muscle. It does not seem, however, that new muscular tissue is produced. With regard to nerve and bone this is different; repair terminates in regeneration, and new tissue may be produced which is identical with

the original tissue. Regeneration occurs in but few tissues; the nerves and bone are the best examples. Repair seems possible in almost any tissue, but such repaired tissue may be functionally inactive, because regeneration has not been complete. Thus, a large cicatrix upon the skin does not contain sweat-glands or hair-follicles, and while it protects the subcutaneous tissues, it performs none of the special functions of the skin. Destroyed kidney tissue may be followed by repair, but apparently not by regeneration.

Regeneration of nerves is now an admitted possibility. In order, however, for the regeneration to be complete, the severed ends of the nerves must be approximated as nearly as possible. At the end of about four days segmentation of the myelin sheath occurs, with fragmentation of the peripheral part of the nerve. At the end of a week proliferation of the neurilemma begins; new cells migrate into the spaces between the severed ends of the nerves. By the end of the second week the axis cylinder, as well as the myelin, have disappeared. In the meantime the fibrous growth of the sheath has extended, and the new fibers are projected through the embryonic elements and join the two severed ends. At first the new fibers are amyelinic; later, a sheath develops, changing them into myelinic fibers. While it requires several weeks for the process to be completed, still, conductivity may be partially established in much less time. Thus, Kenneday has reported a case in which suture of the median and ulnar nerves, six and one-half months after division, was followed by evidences of conductivity in three days, localization of touch in nineteen days, and complete return of sensation in one month. Motion was more slowly regained, and not fully at the end of several months.

Regeneration of Bone.—Immediately following the fracture, hemorrhage occurs from the marrow into the surrounding tissue, and infiltrates the spaces between the bone, under the

periosteum and the adjacent lacerated tissue. Immediately following this, a large number of the leukocytes enter the blood-clot. The red blood-cells break down or are destroyed by the phagocytes, and proliferation of the connective-tissue cells, derived partly from the osteogenetic layer of the periosteum, occurs. While the production of embryonic tissue is progressing, we have the osteogenetic layer of the periosteum giving rise to osteoblasts, which infiltrate the embryonic callus-forming elements; these stellate osteoblasts are later produced from the bone and bone-marrow, and through them the regeneration of the bone, in its ultimate histologic structure, occurs. The time involved varies; it may be considered as reasonably sure that bone formation has taken place before the end of the second week or the beginning of the third. The infiltration of lime salts into the bone-forming elements first occurs along the periosteal layer from which the original osteoblasts arose. If accurate coaptation of the ends of the bone has been secured, the formation of the medullary canal will be reasonably rapid. If, however, the ends overlap, the process is much slower, the two ends being covered by bone, and the canal can only be re-established after the absorption of the sides of the bone at the point of contact. This requires months or often years, and by some it is held that, where the nutrition of the bone is supplied by nutrient vessels above and below the seat of union, the establishing of the canal may not occur.

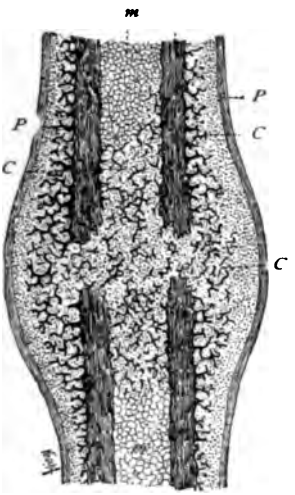


FIG. 109.—TEN-DAY-OLD FRACTURE.—(*Schmaus.*)

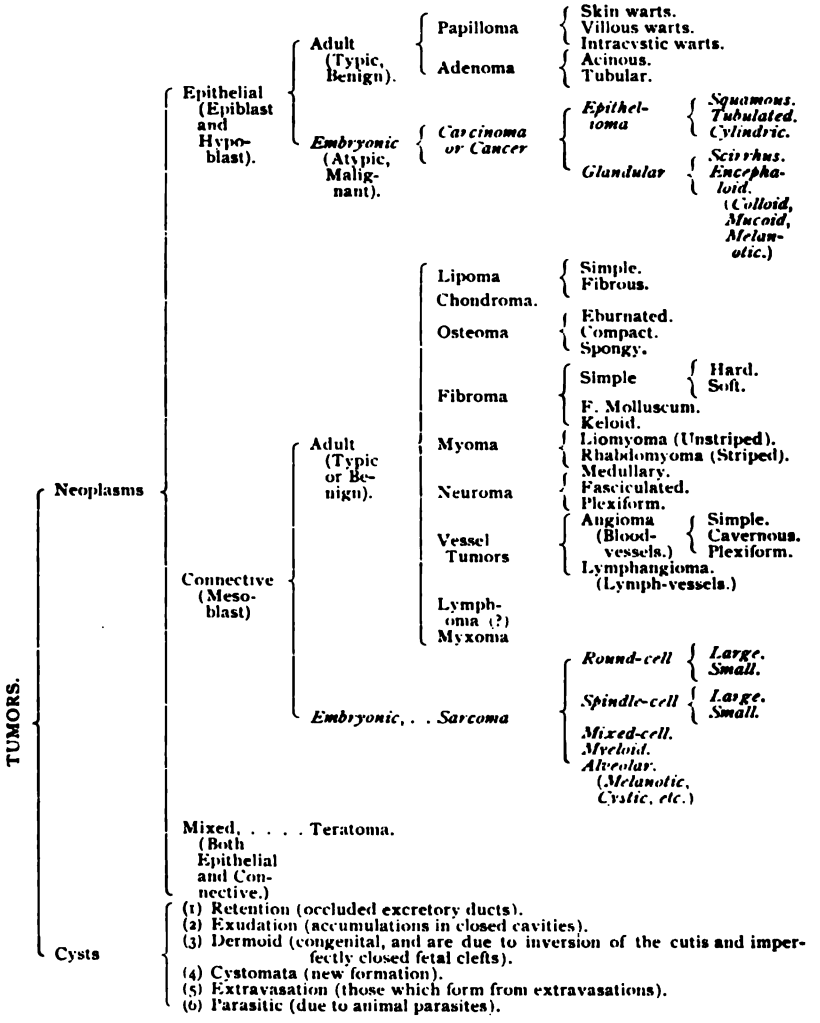
m. Bone marrow. *P*. Partially displaced periosteum. *C*, *C*, *C*. Deposit under the periosteum and extending between the ends of the 2 fragments and into the medulla.

QUESTIONS.

(1) What is inflammation? (2) To what is it most commonly due? (3) What changes occur in the blood-vessels during inflammation? (4) What changes occur in the blood current during inflammation? (5) What changes occur in the perivascular tissues? (6) What is the cause of (*a*) heat, (*b*) pain, (*c*) discoloration, (*d*) swelling, (*e*) disordered function, and the systemic phenomena seen in inflammation? (7) What is repair? (8) Describe the methods by which cells reproduce themselves. (9) Give forms of union in wounds. (10) How does regeneration differ from repair? (11) Describe regeneration of nerves. (12) Describe regeneration of bone. (13) What forms the wall of an abscess? (14) What is embryonic tissue? (15) What is granulation tissue? (16) What is pus?

TUMORS.

(Those printed in *italics* are malignant.)



CHAPTER VI.

TUMORS.

The word *tumor*, which means *swelling*, has been variously applied in medical literature.

Tumors are divided into (1) Neoplasms; (2) Cysts.

A **neoplasm** is a pathologic new growth, having a tendency to persist or to increase independently of the structure in which it lies, and which is without physiologic function. A tumor, therefore, differs from an *inflammatory enlargement* by its tendency to persist and enlarge, while inflammatory new formations tend to disappear or reproduce the tissue of their matrix. Besides, inflammation has marked clinical phenomena and not infrequently an assignable exciting cause.

A *hypertrophy* differs in the fact that it is a result of increased physiologic demands or of a local nutritive change, and that it tends to subside after the withdrawal of the exciting cause. Also, as a rule, hypertrophy does not destroy the natural contour of a part, while a tumor does. Hypertrophy is associated with increased functional power.

General Considerations.—For purposes of clinical description and pathologic study there are certain terms used in connection with tumors with which the student should be familiar. In studying the tumor either for diagnostic or pathologic purposes, there should be always a definite routine in the method of examination, as we have already insisted upon when considering postmortems. The following order is commended: (1) Describe the tumor; (2) its relation to surrounding tissue and organs; (3) the history of the tumor; (4) the history of the patient. In purely clinical studies it is common to begin

with the history of the patient, and the above order may be reversed without altering its usefulness. In describing the tumor, the following points may be of aid in diagnosis, and ought to be developed in the history: (*a*) Its *situation*, superficial or deep, on epithelial or connective-tissue surfaces, or within a structure composed of one or both tissues; this includes the organ involved. (*b*) The *conformation* of the tumor: Is it globular, flat, bossed, pendulous, pedunculated, pyriform, conic, excrescent, polypoid, dendritic, sessile, cauliflower, etc.? (*c*) The *size* of a tumor may be approximately estimated before the tumor is removed from the body, the *weight* afterward. (*d*) *Number:* Is the tumor single—that is, solitary—or is it multiple? If multiple, was it so from the beginning, or was one tumor followed by a succession of others? Are all of the tumors apparently alike, having the same conformation, consistency, and similar location? (*e*) *Consistence:* Some tumors are so soft that they fluctuate; others are *semisolid*, *gelatinoid*, *solid*, *hard*, or even *eburnated*. (*f*) *Color:* This includes the color of the overlying structures. The tissue covering a tumor may be normal or inflamed; it may have tortuous veins; it may be edematous, or even pigmented; it may be so vascular that the color is of a blood tint, either pink or red, or, in some instances, cyanotic. (*g*) The *mobility* of the tumor: Is the tumor movable in the tissue which surrounds it? Is it only movable with the organ involved, or has the tumor, as well as the organ involved, become attached to adjacent tissue? (*h*) *Sensibility:* Is the tumor painful, tender, sensitive to changes in temperature or other atmospheric conditions? is the pain or tenderness constant, remittent, or intermittent? (2) The *influence of the tumor, if any, upon surrounding structures:* Are they involved, inflamed, edematous, sensitive, or anesthetic? (3) The *history of the growth:* How long has the tumor persisted? Is it growing rapidly or slowly? Has its growth been constant or intermittent? Is its growth influenced by any of the functions

of the body? (For example, some tumors in women enlarge during menstruation.) What *pathologic processes*, if any, is the tumor undergoing? Is there evidence of inflammation, gangrene, cyst formation, suppuration, infiltration, or degenerative processes? (4) History of the patient—*Age:* Some tumors appear in the young, others are more frequent in middle life, and some in the old. *Sex:* Some tumors are more frequent in the male; others in the female. *Social condition:* Married or single. *Occupation*, *e. g.*, chimney sweeper's cancer. *Habits:* Some tumors are dependent, apparently—to a certain extent, at least—upon given habits, *e. g.*, smoker's cancer. *Heredity.*—There is reason to believe that in some tumors inheritance may play a part. The history of the *general nutrition of the body:* Has that been influenced in any way, and is the influence purely mechanical, such as may result from the weight of the tumor, or is it attributable to the position? Have ulceration or infectious processes modified general nutrition? In the absence of any other explanation, it may be inferred that the tumor itself has been prejudicial to the patient's health. *Previous history of the organ or tissue involved:* Is there a history of injury or inflammation, such as might occur in the breast during lactation? Has there been any *previous disease of the gland* or *structure involved*, such as eczema? Lastly, but by no means least important, one should obtain the patient's own views upon the case, and the history of the cause, independent of any information which he may have elicited from outside sources.

Causes.—The causes of tumors are largely theoretic. The **inclusion theory of Cohnheim** supposes that there is an excess of embryonic cells necessary to construction of the fetal tissues, and that these masses of latent embryonic cells may be stimulated to active proliferation later in life.

Heredity.—This is by no means always apparent. At most, hereditary influence can only predispose.

Injury and **inflammation** are without doubt exciting causes in a small percentage of cases; more particularly is this true of sarcoma. Persistent or long-continued irritation seems to favor the development of epithelioma, while trauma, or suddenly applied injury, followed by inflammation, favors sarcoma.

Age.—*Physiologic activity* favors the development of sarcoma, while *physiologic decline* favors the development of cancer (Da Costa).

Parasitic Influence.—The characteristics, method of growth, processes of dissemination, and the life history of malignant tumors, point to a possible infectious agent being their cause. In the cancers there has recently been described as constantly present an animal parasite belonging to the group of protozoa; its exact etiologic significance has not been definitely settled.

Neoplasms are subject to two general laws: (1) **Müller's Law**: *The tissue which forms the tumor has its type in a tissue of the organism, either adult or embryonic.* By this is meant that, no matter what the cellular elements of a tumor may be, such elements occur as normal structures in the adult tissues or in the tissues of the embryo at some period of its development. (2) **Virchow's Law**: *The cellular elements of a tumor are derived from the pre-existing cells of the organism.* He also adds that they are derived from the cells of the connective tissue—a view not to be fully accepted.

By the acceptance of these two laws we establish that tumors spring from structure once normal, and represent, when fully developed, tissues which were once normal; in other words, tumors are not importations into our bodies, but, like all other morbid processes, are perversions of normal cellular activity.

Tumors, in a general way, obey the laws which regulate normal tissue, yet to some extent they live independently of the surrounding tissue. They usually possess their own cir-

culation, and disseminate and proliferate at the expense of the adjacent tissue. While the nutrition of the patient may not be sufficient for the development and maintenance of high-grade adult tissue, wasting of the normal tissue elements constantly progresses, and the tumor cells may proliferate with alarming rapidity.

Tumors are said to enlarge or extend either by (*a*) **interstitial growth** or by (*b*) **dissemination.** By the former is meant that the growth within the tumor is uniform; that it increases in size by proliferation of its cells without any dislodgment except that incident to one cell pushing another during the process of multiplication. Such tumors are likely to form capsules, the **capsule** developing either as a part of the tumor cells or by condensation of the surrounding tissue. The simple non-malignant tumors may have capsules formed in either of the two ways indicated, but the malignant tumors are less likely to have anything like a capsule by reason of the fact that they grow largely by dissemination.

(*b*) **Growth by dissemination** is said to be (1) **growth by infiltration**; (2) **growth by metastasis.**

(1) **Local dissemination** or **infiltration** is an extension of the tumor into the surrounding tissue; this usually occurs by the tumor cells entering into the lymph-spaces. Tumors growing by infiltration have no sharply defined border, and are, therefore, without any capsule, thus rendering the surgeon unable, in their removal, to definitely determine exactly how far it is necessary to go in order to remove all of the tumor tissue.

(2) **Metastasis.**—When, as indicated above, the tumor cells infiltrate the primitive lymph-spaces, it will be seen how easy it is for such infiltrated cells to be caught in the lymph stream and carried to the glands into which the lymphatics of the area involved empty; such extension is most common in cancers, although it may occur in sarcoma, and is known as **metastasis by the lymph stream.**

Metastasis by the Blood.—In certain forms of tumors, particularly in the sarcoma, there is no attempt at well-formed blood-vessels, as will be seen later; the blood traversing such tumors passes through what may be called sluice-ways, the walls of which are not uncommonly formed entirely of tumor cells. These cells may drop off into the blood stream and be carried along as emboli, reproducing the tumor wherever they lodge. Again, a tumor may involve a blood-vessel by extension; that is, it may infiltrate the wall of the blood-vessel, project into its interior, and small fragments break off, which may be carried to distant parts. The walls of the veins being thinner than those of the arteries renders infiltration easier and more disastrous, as they may assume wider dissemination than would be possible if only the artery was involved.

Pigmentation which occurs in tumors may be due to hemorrhage within the tumor and the breaking down of blood-coloring matter, or may be due to the fact that the tumor produces a pigment, such as seen in the chloroma, melanotic sarcoma, and a few other tumors. It may also be due to the development of certain bacteria, particularly if the tumor be ulcerated.

Classification.—Clinically, tumors are said to be (*a*) **benign** or (*b*) **malignant.** By the former it is meant that the tumor of itself does not necessarily involve danger to life, while the latter implies that, if left alone, the tumor will eventually prove fatal. A tumor ordinarily innocent or benign may destroy life simply by its location; for example, a fibrous tumor growing on the inside of the skull. This, however, does not entitle fibrous tumors to be classified among the malignant, as its proving fatal in the particular instance cited is what Park has termed "malignancy by accident of location."

At one time it was quite the habit of clinicians to classify tumors according to some peculiarity of shape or physiology. As examples of this, we have scirrhus, for hard, and en-

cephaloid, for soft; again, bleeding tumors, when fungoid, all came under the one head, "fungus hematodes." The broadening of our knowledge as to the minute structure of tumors has led to a classification upon their morbid histology and histogenesis.

Classification Based on Histogenesis.—While authors differ in their classification of neoplasms, yet, if we grant the law of Müller, our classification must be based solely upon the analogy of tumors with the normal tissues, either in the adult or embryonic state. All tissues spring from one of two types: (1) *Epithelium;* (2) *Connective.* Tracing these back to the blastodermic layers, they are developed as follows:

(1) *Epithelium*, from the epi- and hypoblastic layer (or upper and inner layer) of the blastoderm. (2) *Connective tissues*, from the mesoblast (or middle layer) of the blastoderm. All neoplasms spring from one of these two types, each type of tissue having two varieties:

(1) **Epithelium**: (*a*) *adult* or *typic;* (*b*) *embryonic* or *atypic.*
(2) **Connective**: (*a*) *adult* or *typic;* (*b*) *embryonic* or *atypic.*

By *adult* or *typic* tumors we mean those which have their type in the then existing adult body, and are, *clinically, benign.*

By *embryonic* or *atypic* tumors we mean those which have no type in the adult body, but revert to the embryo for their prototype, and are, *clinically, malignant.*

EPITHELIAL TUMORS.

ADULT EPITHELIAL TUMORS.—(1) **Papilloma.**—These growths are formed from cutaneous and mucous papillæ, and consist of a fibrous stroma containing blood-vessels and lymphatics, with an epithelial covering of the same variety of epithelium as that of the diseased part. The histologic structure of a papilloma is the same as that of the ordinary papillæ, and consists of a basis of connective tissue, richly cellular, from which project toward the surface numerous papillary

processes, each process supporting blood-vessels which end in a capillary loop, the whole being enveloped in a covering of epithelium.

The papillæ vary in length; in the ordinary wart they are short; in the *villous papilloma* they appear as long, delicate fibrils, giving off secondary and tertiary shoots.

The epithelial covering is thick, hard, and stratified, and actually binds the papillæ into a solid mass; on mucous membranes the slender vascular processes are covered with epithelium very delicate and easily lacerated.

Site.—Papilloma may appear anywhere on the skin or mucous membrane; as a rule, they grow from pre-existing papillæ; rarely do they occur where no papillæ exist; in such cases they spring directly from the subepithelial connective tissue—this is the case in the *stomach and larynx.*

FIG. 110.—PAPILLOMA. —(*Gould.*)

Physical Characters.—Ordinarily papilloma appears as a hard, abruptly elevated mass, apparently of epithelium, presenting an irregular or "warty" surface, usually divided by deep fissures; the length of the papillæ, with the depth of the fissures, determining the variety. On section, the relation between the stroma and epithelium may be seen even with the naked eye.

Clinical Characters.—Clinically, warts are benign or innocent. They may occur at any age; may be single or multiple; may disappear without any operative interference: this is especially true of multiple warts. When occurring on mucous surfaces they are highly vascular, and owing to their thin epithelial covering cause much trouble, and even death, by bleeding. This is especially true in the bladder and urethral orifice. In the young, warts are occasionally transformed into sarcomata; in advanced life there is a tendency of warts

and warty surfaces (ichthyosis linguæ) to become carcinomatous.

Varieties.—(1) Skin warts; (2) villous; (3) intracystic warts.

(1) **Skin Warts.**—(See Fig. 110.) Skin warts are overgrown papillæ, and on section the epithelium will be found to pass from one papilla to another in an unbroken line without invading the fibrous framework. They vary in size, and may become mottled with black pigment (melanotic).

FIG. 111.—PAPILLOMA WITH TENDENCY TOWARD VILLOUS FORMATION.—(*Schmaus.*)

(2) **Villous Warts.**—These commonly spring from the mucous membrane, usually of the bladder and occasionally of the renal pelvis; the condition is termed "*villous disease.*" The general appearance of the long, branching, feathery tufts resembles the delicate chorionic villi; structurally, the villi consist of a connective-tissue core traversed by delicate blood-vessels, the whole being surmounted by epithelium. They may be *single* or *multiple*, sessile or pedunculated.

(3) **Intracystic Warts.**—These may occur within almost

any cyst cavity lined by epithelium, more especially those formed in glands; *e. g.*, mammary cysts, thyroid cysts. The intracystic warts are in structure the same as the villous.

(II) **Adenoma.**—An adenoma is a tumor constructed upon the type of a gland, but does not produce secretion. Adenomata are of slow growth, and believed to have their origin in some quiescent, congenitally displaced rudiment; their ducts do not communicate with the normal gland; they are completely encapsulated, thus distinguishing them from localized hypertrophies. Clinically, they are benign. The secondary changes are fatty degeneration of the epithelium, dilatation of the saccules and tubules into cysts, and mucoid softening. Containing both connective and epithelial cells, transformation into sarcoma and into carcinoma is possible, — the former is most frequent in the young, and the latter in the aged.

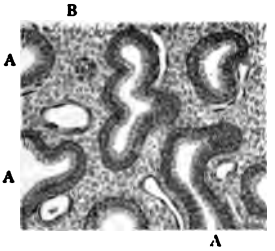


FIG. 112.—ADENOMA, TUBULAR.—(*Gould.*)

A, A, A. The acini lined by columnar epithelium. B. The fibrous network or basement substance.

Site.—They may develop in any glandular structure or in any tissue containing glandular structure. The chief species of adenoma are: Mammary, sebaceous, thyroid, prostatic, parotid, hepatic, renal, ovarian, testicular, gastric, intestinal, fallopian, and uterine.

Varieties.—(1) *Acinous;* (2) *tubular.*

(1) **Acinous Adenoma.**—(See illustration.) This variety consists of numerous saccules or acini lined with small epithelial cells, which are often two or three layers deep. The acini communicate and are grouped together, being separated merely by a connective tissue in which are situated the blood-vessels. The connective tissue or fibrous stroma varies in amount; when in excess, the tumor is known as a *fibro-adenoma.*

(2) **Tubular Adenoma.**—This variety is very common in the mucous membranes which possess tubular glands. They are usually soft, slightly translucent, and somewhat vascular. The tubes are lined with cylindric-cell epithelium. On section, when cut transversely, the tubes appear as circles, with a central lumen and a border of regular cylindric epithelial cells. When cut longitudinally they often show lateral buds, or even bifurcations terminating at one end in the mucous membrane, where they open; at the other, in blind sacs situated at varying depths; these tubes may be so closely packed together as to show almost no fibrous stroma; the cylindric cells which line the tubes are usually two or three times as long as normal. This variety of adenoma is prone to undergo malignant transformation, many of the cancers of the rectum and uterus arising from this tumor.

EMBRYONIC EPITHELIAL TUMORS.—**Carcinomata**, or cancers, are embryonic or atypic neoplasms, which do not have their type in adult epithelial cells, but revert to the embryo for their prototype. They always develop from the *epithelial* cell, which cell becomes abnormal in form and, if growing in glands, fills up the lumen of the gland's tubule, acinus, etc., penetrating the basement or limiting membrane, and infiltrating the lymph-spaces of the connective tissue. Carcinomata are really epithelial cells out of place.

Histology.—In carcinoma we have two essential elements to describe: (1) the *epithelial cells;* (2) the *stroma* which bounds the space in which the epithelial cells lie, the space being known as the *alveolus.*

Cells.—The cells are characterized by every diversity of outline; they may be round, oval, squamous, fusiform, or caudate, and with prominent nuclei and nucleoli. The nuclei may be single or multiple, but are always large and prominent. The variation in form of the cell is due to the pressure to which they are subjected in the process of their arrangement

and proliferation, and to the shape of the cell from which the cancer arose.

The cells are loosely nested in the alveoli, and do not attach themselves to the fibrous stroma. Being of a low grade of tissue, they rapidly undergo retrogressive changes, and not uncommonly contain molecular fat.

Fibrous Stroma.—The amount of fibrous stroma varies; it consists of distinctly fibrillated tissue arranged so as to form the *alveoli.* These alveoli communicate with one another and form a continuous cavernous system distended by the epithelial cells.

The character of the stroma depends largely on the rapidity of growth. If rapid, it will contain some round and spindle-shaped cells; if the growth has been slow, or has ceased altogether, the tissue will contain few or no recent or round cells, and will be more dense and fibrous in character. The latter is the most common condition in scirrhus, the former in encephaloid. Situated in this stroma are the blood-vessels, which are limited to the stroma, and do not pass into the epithelial masses; they have distinct and thickened walls. This is one of the distinguishing features of carcinomata—the vessels having a distinct fibrous wall, and the nests of epithelial cells not attaching themselves to the fibrous stroma. The lymphatics communicate freely with the alveoli, which accounts for the frequency of infection of lymphatic glands. It is through these channels that carcinoma spreads.

Clinical Characters.—As a rule, carcinoma occurs after thirty-five. The growth is usually primarily single. Generally the growth is hard. The so-called soft cancers are those which have undergone some secondary change, as fatty or colloid, or are made up of epithelium in excess, as the encephaloid. Cancers tend to infiltrate adjacent connective tissues. There is usually a central tumor mass, from which processes are seen radiating into the surrounding tissue. The border of the

tumor is not sharply defined; the typic connective- and epithelial-tissue tumors, on the other hand, are likely to have well-defined margins, and can be, in most instances, enucleated from the tissues in which they lie. Carcinoma has no capsule, and can not be enucleated. The tendency is to ulceration.

Secondary carcinoma is usually multiple, has a more sharply defined or circumscribed border, and, while it projects into the neighboring tissues, it does not tend to infiltrate them in the same manner as in the primary tumor, and, as a rule, the mass is much softer. These conditions are probably due to the recent character of the growth.

Secondary Changes.—The most important are certain forms of degenerative change, among which is fatty degeneration. This depends somewhat on the rapidity of the growth; the more rapid the growth, the more rapidly this change takes place, hence it is usually most marked in the encephaloid. Among the other secondary changes which are liable to occur are: hemorrhage, mucoid and colloid degeneration, pigmentation, or melanosis. Among the rare secondary changes are: cyst formation, calcification, ossification, very rarely abscess formation, and gangrene.

Site.—Anywhere where there is epithelium, different varieties being peculiar, to a certain extent, to different tissues.

Varieties.—(I) Epithelial carcinoma; (II) Glandular carcinoma. The term epithelioma is used in a broad sense by some writers as referring to all carcinomata. It is here applied to those varieties of carcinoma which spring from epithelial surfaces, and is often spoken of as superficial cancer.

(I) **Epithelioma** assumes three types:

(1) *Squamous cell;* (2) *cylindric cell;* (3) *tubulated.*

(1) **Squamous Epithelioma.**—This variety always grows from a surface covered by squamous epithelium, either cutaneous or mucous; its epithelial elements closely resemble squamous epithelium; the distortion in shape of the cell is due

to the pressure to which it is subjected during its growth. The cells penetrate from the surface epithelium into the lymph-spaces of the connective tissue, and follow those channels which intercommunicate. Occasionally single isolated epithelial cells may be recognized in the connective tissue of the growth. Transverse sections of the epithelial masses show typic nesting of cells, the so-called *concentric globes* or *epithelial nests.* When these nests undergo hardening, a change incident to age and attempted desquamation, they are spoken of as "*pearls*," hence the term *pearl*

FIG. 113.—SECTION OF A SQUAMOUS EPITHELIOMA.—(*Kindfleisch.*) × 500 diameters.

a. The down-growing epithelium in which are two cell nests or pearls. *b*. The stroma, in which, at *c*, a few round-cell elements are to be seen.

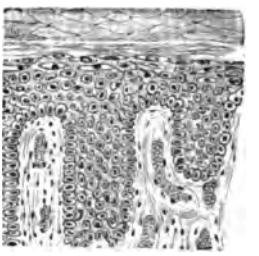


FIG. 114.—SQUAMOUS EPITHELIOMA.—(*Gould.*)

epithelioma. The fibrous stroma may show some inflammatory infiltration, particularly if the ulceration incident to softening and infection has occurred. It shows little of the alveolar arrangement which characterizes some of the other varieties of carcinoma. The ulceration which occurs early may not be due to an inflammatory process, but to fatty degeneration of the cells.

The growth usually begins as a small, hard ulcer, or an

indurated tissue, or possibly as a subcutaneous induration or nodule which tends to early softening, infection, and ulceration. When fully developed it presents an irregular, ulcerated, warty-looking appearance, exuding from its surface at times a clear, or slightly tinged, or, it may be, an irritating, ichorous fluid. The ulceration occurs in the center, surrounded by an indurated area beyond which may be firm and distinct nodules. On section the tumor is firm, and the fibrous stroma may show as white glistening bands. As a rule, there is no hemorrhage; there are few blood-vessels near the surface. The process develops slowly, and glandular involvement may not occur for years, although in rare instances it has been observed within the first year.

Site.—Squamous epithelioma usually occurs at the junction of the skin and the mucous membrane, or where two kinds of epithelium join. It is frequently found on the lower lip, nose, penis, scrotum, vulva, anus, tongue, less commonly on the gums, palate, tonsils, larynx, pharynx, esophagus, bladder, os uteri, general cutaneous surface; rarely on the hands and feet.

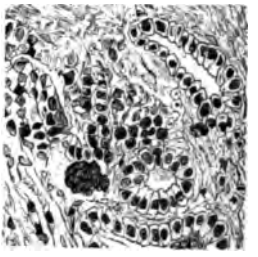


FIG. 115.—CYLINDRIC- OR COLUMNAR-CELL EPITHELIOMA. —(*Gould.*)

(2) **Cylindric-Cell Epithelioma.**—(*Adenoid cancer, columnar-cell epithelioma, malignant adenoma.*)—This variety is characterized by irregular or tubular cavities, paved with one or more layers of cylindric cells, and separated by a stroma which may be fibrous, embryonal, or mucous. In structure it occupies an intermediate position between the simple adenoma and true cancer. The cylindric cells are similar to those which cover certain mucous or glandular cavities, and are always implanted perpendicularly to the wall. The epithelial elements are similar to those of the mucous membrane from which they grow, but

differ microscopically from the normal mucous membrane in the absence of a basement membrane (membrana propria). The slower the growth, the more typic the gland formation; in rapid growths and recurrences the cells are small and the lumina imperfect. The growths are soft, and often of a gelatinous consistence. On section they present a soft, watery appearance. The most common forms of degenerative changes are mucoid and colloid.

Age.—Cylindric-cell epithelioma, as a rule, occurs earlier than any other variety of epithelioma; its growth varies, may be rapid or slow, usually rapid.

Glandular involvement, or metastasis, usually occurs early and progresses rapidly.

Site.—Rectum (in the rectum it may occur very early in life), stomach, uterus, ovary, gall-bladder, biliary passages, and respiratory tract; may occur in any portion of the intestine.

As secondary growths, this variety of cancer occurs in the lymphatic glands, liver, lungs, kidney, and bone; if secondary, it possesses the same characteristics as the primary growth.

(3) **Tubulated Epithelioma,** also variously known as *rodent ulcer, tubular epithelioma, noli-me-tangere, lupus exedens, herpes exedens*, etc.—This form of epithelioma is composed of pavement epithelium, arranged in plugs or cylinders, anastomosing with one another, and imbedded in a stroma, which consists of embryonal, mucous, or fibrous connective tissue. These tumors appear as spheric or ovoid masses. Upon section they represent gland structure, but yield no fluid on pressure. Under the microscope these tumors consist of anastomosing cylinders made up of pavement epithelium, surrounded by a variable stroma, which is usually fibrous and very dense. When mucous, it is more likely to undergo degeneration and become cystic or colloid. The development is usually slow, and may be arrested and remain stationary for

a considerable time; again, without any apparent reason, the tumor may suddenly assume a most rapid growth.

Glandular involvement is more uncertain in these cases than any other class of cancer; in some instances the spread is rapid, in others slow, in some cases never appearing. When upon the mucous surfaces or upon the eyelid, the growth is likely to be rapid.

Site.—Most frequent location is on the face, tongue, general cutaneous surface, intestine, uterus, and ovary. When occurring in the skin, the mass is believed to develop from the sudoriferous glands, or, possibly, the hair sheaths.

(II) **Glandular Carcinoma.**—Varieties: (1) *Scirrhus;* (2) *encephaloid.*

(1) **Scirrhus** (*Acinous cancer, chronic cancer, hard cancer, fibrous carcinoma*).—This variety of carcinoma is characterized by the amount and density of its stroma, and by its irregular growth. The tumor occurs as a hard, firm mass, varying in appearance according to its location. In the breast, which is its common site, it forms a hard rounded or irregular mass, which soon becomes firmly attached to the subcutaneous tissue, and eventually to the skin. By the contraction of the fibrous stroma it causes retraction of the nipple and puckering or dimpling of the skin—"bacon-rind" skin.

FIG. [illegible]—SCIRRHOUS CARCINOMA. HARD CANCER.—(*Gould.*)

A. Fibrous stroma. B, B. Cancer cells (epithelium), occupying the alveoli.

On section it presents a grayish-white glistening appearance, dotted with yellow patches of fatty tissue. The fibrous bands and fatty areas are more marked toward the center of the tumor. Toward the periphery it is more vascular and less fibrous; it is non-encapsulated. On microscopic section the tissue is composed of two structures, connective tissue and

epithelial cells, the connective tissue or stroma being arranged so as to form a series of rounded or irregular spaces (alveoli) in which the epithelial cells are nested. The blood-vessel walls are thickened and fibrous. Microscopic section from the central part of the tumor will show the connective tissue more dense and fibrous and the alveoli much smaller, with the epithelial cells small and atrophied, or possibly degenerated. With the increase in the fibrous stroma there is increased contraction, causing irregularities of the surface; when occurring in the breast, this contraction gives rise to retraction of the nipple—umbilication.

The forms of degeneration which are likely to occur are fatty, colloid, mucoid, hyaline, and, rarely, caseous necrosis. Melanotic, or pigmentary, and calcareous infiltrations occur.

Glandular involvement usually takes place within the first year.

Site.—Most common in breast, uterus, stomach (pylorus), esophagus, rectum, and kidney; rare in ovary, testes, and prostate.

Atrophic Scirrhus.—When the production of fibrous tissue predominates and the epithelium proliferates but slowly, the resulting tumor contracts more rapidly than it grows. The epithelial cells are therefore pressed upon, and often disappear from many areas. This form of scirrhus is a breast tumor, and, once developed, it is most commonly found that the gland and tumor progressively diminish in size. The malignancy is low, and if the fibrous tissue development persists in its excess, the patient rarely succumbs. The writer had a case under observation, a woman seventy-two years of age, who had refused an operation nearly twenty years previously. The entire breast of one side, and the overlying and adjacent skin, showed puckering and contraction; the breast of the other side was also invaded, but ulceration had not taken place over either gland.

Glandular involvement may be long delayed, or, in a few cases, may not occur. In the case just mentioned there was very slight involvement only in the last few years. The patient died at seventy-four, of erysipelas.

Microscopically, such tumors are mostly stroma, with few alveoli; the contained epithelial cells are advancedly atrophied, degenerated, or both.

(2) **Encephaloid** (*Medullary carcinoma, soft cancer, acute cancer*).—This rare variety of carcinoma is a soft, rapidly growing, brain-like tumor, in which the fibrous stroma is more nearly

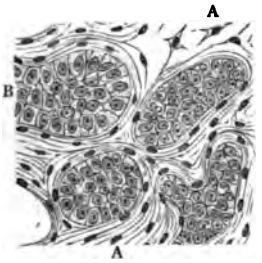


FIG. 117.—ENCEPHALOID CARCINOMA (SOFT CANCER).—(*Gould.*)

A, A. Stroma made up of developing connective tissue. At the upper A the stroma is almost myxomatous. B. Epithelial cells occupying an alveolus; three other alveoli are shown.

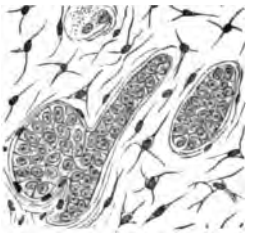


FIG. 118.—GLANDULAR CARCINOMA, IN WHICH THE STROMA HAS BEEN CONVERTED INTO MUCOID TISSUE.—(*Gould.*)

Note the stellate cells so closely resembling those seen in the myxoma.

embryonic, not uncommonly myxomatous, and very scanty, the alveoli large, and filled with large, rapidly growing epithelial cells. It appears as a soft, at times almost fluctuating, nodular mass, which tends to ulcerate and bleed (fungus hematodes). There is early involvement of the skin ("bacon-rind"), soon followed by superficial necrosis and ulceration. As a rule, encephaloid occurs earlier in life than scirrhus, and has been reported in the young. It may occur as a primary or secondary growth. The growth is excessively rapid, and glandular involvement early—within the

first six months. There is no retraction of the nipple when occurring in the breast, and the rapidity of growth produces a more markedly circumscribed mass than scirrhus; it is, however, more rapidly fatal.

Site.—Primarily, most common in mammary gland and testes; may occur as a secondary growth following scirrhus, but frequently occurs in internal organs. Is much less common than scirrhus.

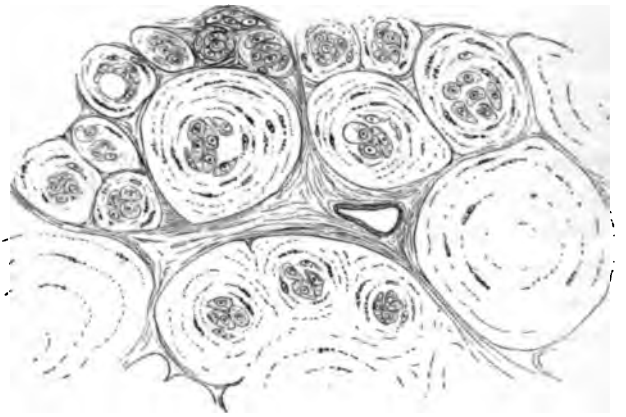


FIG. 119.—COLLOID CANCER.—(*Rindfleisch.*) × 300 diameters.
The stroma has been but little involved, while the intra-alveolar structure has been converted almost entirely into colloid material.

Colloid or **gelatiniform carcinoma** is a carcinoma in which degeneration takes place in the protoplasm of the epithelial cells which occupy the alveoli, a process which may develop in any variety of the carcinoma, especially the glandular; the epithelial cells are converted into a peculiar gelatinous, semi-transparent substance. (See "Colloid Degeneration.") The alveolar structure in the colloid carcinoma is very marked, the fibrous stroma is very thin, and the blood supply limited. Chemically, colloid carcinoma differs from mucoid carcinoma in containing sulphur, and in not being precipitated by acetic acid and alcohol.

Mucoid Carcinoma.—When the substance which distends the alveoli is more viscid in character, it is referred to as a mucoid degeneration of the intercellular substance, more than a colloid change commencing in the cell. It is the transformation of the albuminoid constituents of the tissue into *mucin*. Chemically, it is closely allied to albumin, but differs in not containing sulphur; it is soluble in acids, insoluble in an excess, and is not precipitated by boiling, by tannin, or bichlorid of mercury. Cause not known. (See "Mucoid Degeneration.")

CONNECTIVE-TISSUE TUMORS.

ADULT CONNECTIVE-TISSUE TUMORS.—(I) **Lipoma.**—Varieties: (1) *Simple;* (2) *Fibrous.*

A lipoma or fatty tumor is a localized, circumscribed new formation of fat. It is lobulated, soft, doughy, pseudofluctuating, and inelastic. As to shape, it is ovoid, spheric, or flat, usually sessile, rarely pedunculated. If encapsulated, the capsule is exceedingly thin: the growth is usually single; if multiple, as a rule it is hereditary. Microscopically, fatty tumors consist of cells containing fat and a variable quantity of connective-tissue stroma. The cells are like those of adipose tissue, though usually larger. The blood-vessels are distributed in the fibrous stroma. If the fibrous tissue is in excess, it is spoken of as a **fibrolipoma** or fibro-fatty tumor. The fibrous fatty tumor or fibrolipoma differs from the **simple lipoma** in the amount of fibrous tissue. In the fibrolipoma this is abundant; there is no capsule, and, if the tumor be grasped at its base, the skin made tense, dimpling of the cutaneous covering occurs, due to the fibrous bands which traverse the tumor pulling the skin in at the point of

FIG. 120.—LIPOMA.—(*Gould.*)

their attachment. If in combination with mucous tissue, it is spoken of as a **myxolipoma.**

Clinically, they are benign tumors of slow growth and of variable size.

The degenerations and infiltrations which they may undergo are calcareous, fatty, mucoid, ossification, ulceration, cystic degeneration, and secondary inflammatory and necrotic changes.

Site.—Connective tissue, subcutaneous tissue of trunk, especially of back and abdominal walls; intermuscular septa, subsynovial and subserous tissues, rare in stomach and intestines and internal organs. An interesting phenomenon is the "gravity wandering," occasionally observed in the simple fatty tumor.

(II) **Chondroma** (*Enchondroma, Enchondrosis, Chondroid Exostosis*).—Masses of new tissue, composed either of hyaline or white fibrocartilage, which have for their type normal cartilage tissue. Although cartilaginous, they rarely arise from pre-existing cartilage tissue. They are rounded, smooth, tuberous, or lobulated tumors of very dense consistence, often appear to be encapsulated, due to the compression of the surrounding tissues; not uncommonly, however, they have a well-marked capsule. The cut surface presents a pearly, bluish-pink appearance, identical with fresh cartilage. As a rule, cartilage tumors are non-vascular, but if vascularization occurs it is at the center or through the fibrous septa. Microscopically, they resemble true cartilage tissue; the intercellular substance may be hyaline, faintly or distinctly fibrous, or, in rare instances, mucoid. They are not, as a rule, composed of dense cartilaginous tissue, but of islands of cartilage surrounded

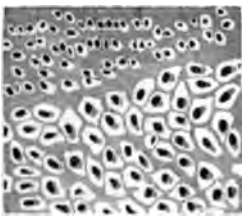


FIG. 121.—CHONDROMA.—(*Gould.*)

by fibrous septa. The cartilage matrix is hyaline except where it joins the fibrous stroma, where it is usually more or less fibrous. Within the matrix are the lacunæ containing the cartilage cells ; these resemble the normal cartilage, and are either rounded or oval in shape. The lacunæ of the matrix are occasionally branched so as to cause the appearance of a series of stellate spaces, with cartilage cells lying in their center.

Infiltrations and Degenerations.—Fatty, mucoid, calcareous (most common), and cystic ; ossification may occur, especially when growing at junction of the epiphysis and shaft of long bones.

Age.—Most common at the age of puberty.

Site.—Bones ; as bones are developed largely out of cartilage, it may be supposed that remnants of the embryonic cartilage are left over and afterward developed into tumors. They occur more frequently on the metacarpal bones and phalanges of the hands ; not so frequently on the analogous bones of the foot. Chondromata are not infrequent on the femur and bones of the pelvis, in the last-named situation not uncommonly attaining the largest size ; frequently on the ribs and scapula ; rarely on the face and skull, sheaths of tendons, and bronchial cartilages ; most rarely in the soft parts, but have been observed in the testicles, ovaries, mammæ, and salivary glands.

(III) **Osteoma.**—A tumor-like mass of bone developed without the occurrence of inflammation or incident to the process of repair; usually occurring at the point of junction between a bone and its cartilage. They are classified, according to their position, into (1) **exostoses,** or those growing from the exterior of a bone, and (2) **enostoses,** or those growing from the interior of a bone. According to their structure they are classified into (1) *eburnated ;* (2) *compact ;* (3) *cancellous* or *spongy.*

(1) **Eburnated Osteoma.**—These occur most frequently

on the inner table of the skull, and are usually syphilitic. They are extremely hard, symmetric, and usually multiple. On section, the dense bony structure is composed of lamellæ, which are arranged parallel with the surface of the tumor. In the lamellæ there are no blood-vessels and no Haversian canals, but canaliculi similar to those found in the cementum of teeth; these run toward the surface.

(2) **Compact Osteoma.**—This variety is composed of ordinary compact bone similar to that found in the outer layer of the long bones. The growth is nodular, usually beneath or in the periosteum, commonly met with in the long bones. On section, it is found to differ from the eburnated osteoma in that the vessels and Haversian canals run at right angles to the long axis of the bone. It has a periosteal fibrous covering, with a layer of small round cells (osteoblasts), and young bone formation in progress beneath. Regular Haversian systems often are clearly defined.

(3) **Cancellous or Spongy Osteoma.**—In this variety the trabeculæ are very thin and not numerous; the medulla is embryonic in character, and appears as a gelatinous mass. In rare cases it is distinctly fibroid. The whole tumor is essentially like the spongy tissue of which the ends of long bones and the bodies of shorter ones are composed.

Clinical Characters.—Osteomata are benign tumors of slow growth, usually arrested with advancing age, and rarely attaining a large size. They are often hereditary and multiple, in which case they usually occur in early life. Osseous growths which exhibit malignant characters are *chondrosarcomata*, or *sarcomata* which have undergone partial ossification or extensive calcareous infiltration.

Secondary Changes.—Osteoma may inflame, become carious, or undergo *necrosis*. Rarely an osteoma may develop into a sarcoma.

Site.—Most common in connection with bone, periosteum,

medulla, or cartilage; may occur in the soft parts of the body, in the brain substance, dura and pia mater, in the pleura, diaphragm, and pericardium, in the skin, choroid coat of the eye, air passages, in tuberculous lungs, around or in glands, in nerve-centers, and tendons.

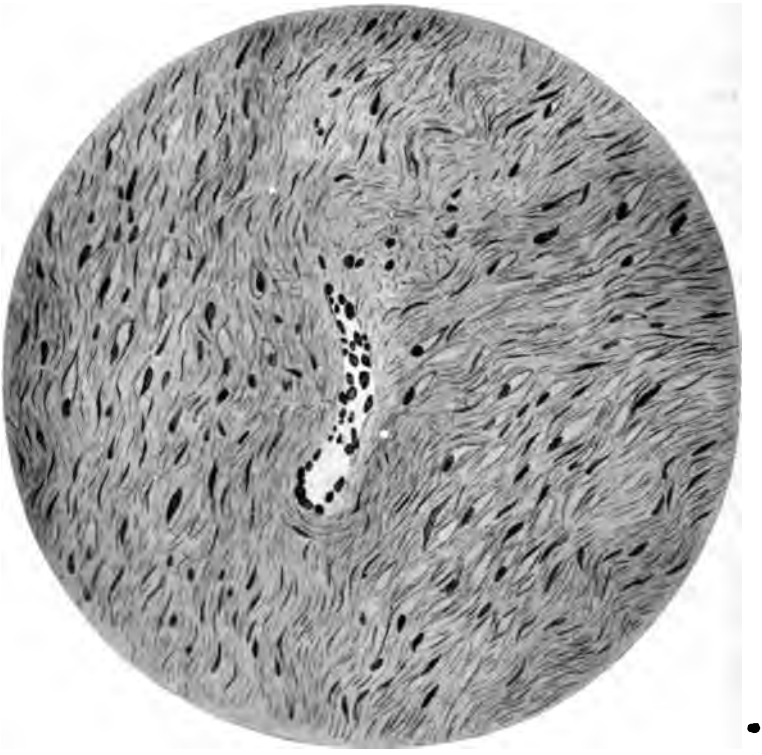


FIG. 122.—SOFT FIBROMA.

(IV) **Fibroma** (*Fibroid, Desmoid, Steatoma, Inoma*).—Varieties: (1) *Simple;* (2) *Molluscum fibrosum;* (3) *Keloid or celoid.*—Fibromata are tumors composed of wavy bundles of fibrous tissues, and have no distinct capsule, though the

surrounding tissue may be so compressed as to simulate a capsule. They are hard and movable, and of slow growth.

(1) **Simple Fibroma.**—This variety is typified in the *painful subcutaneous tubercle* which consists of a tubercle about the size of a coffee-bean in the subcutaneous cellular substance. It is of firm consistence, and is apparently quite circumscribed, being situated loosely in the cellular tissue immediately under the integument. From the extreme pain produced by these small nodules, many have imagined that they must contain nerve-fibers; careful research has failed to demonstrate their existence in all cases. As the myelinic nerve-fiber is almost identical in microscopic appearance with fibrous tissue, we can understand the difficulty which attends the demonstration. They occur more frequently in the female than in the male.

By some authorities fibromata are said to be *hard* or *soft*, the density being dependent upon the degree of development. The hard or dense fibromata are of the type of dense fibrous tissue, while the soft fibromata are of a younger cell growth, and contain fewer fibers and more cellular elements. The hard fibroma is firm, usually lobulated, and encapsulated. The soft fibroma is much less dense, and in texture resembles the lipoma; it may be lobulated or encapsulated.

(2) **Molluscum Fibrosum.** (Synonyms: *Fibrocellular tumor, dermatolysis, and phacydermatocele.*)—This variety of fibroma occurs in a rather extraordinary condition, in which the chief features are the overgrowth of the skin and subcutaneous tissues, which will affect a small area like the scalp, or may involve a large extent of skin on the trunk and limbs, causing it to hang in pendulous folds. Sometimes the tumors form as separate nodules scattered over the skin. Microscopically, the tissue shows as fibrous bundles; intervening are branched cells, the processes which clasp the bundles. In the dense fibrous bands there are few cells. The cells are

almost embryonic in appearance, and contain nuclei of varying sizes.

(3) **Keloid** (*Cheloid, Kelis*).—This is a rare variety of fibroma. It takes the form of tuberous, sausage-like, or discoid growths seated in the corium beneath the papillary layer.

Varieties: (1) *True* or *spontaneous keloid.* (2) *Cicatricial keloid.*

(*a*) **True Keloid.**—This consists of a fibrous growth in the corium, covered with a papillary layer; the papillæ and epidermis are intact; most common in the negro. It consists of bundles of coarse fibers, and in the early stage contains numerous spindle-cells.

(*b*) **Cicatricial Keloid.**—This variety grows in the substance of a scar, and differs from the true keloid in that it is not covered by the papillary layer. In other respects it resembles the true keloid.

Site.—Fibromata originate in connective tissues, cutis, or subcutaneous tissue, from submucous or subserous tissue, from fascia, periosteum, neurilemma, or the connective tissue of organs (uterus, ovaries, testicle, mammary gland, and labium majus). Clinically, they are benign tumors of slow growth, and, with the exception of keloid, do not tend to recur after removal.

Degeneration.—Serous infiltration (as in molluscum fibrosum), mucoid degeneration, fatty degeneration (especially in the simple fibroma of syphilitic origin), calcification, ulceration, and telangiectasis.

(V) **Myoma.**—The myomata are tumors composed of muscular tissue. The tumors vary in size, may be small and rounded, or may attain an enormous volume; are usually lobulated. They are commonly inclosed in a fibrous capsule, and are usually multiple. Microscopically, the muscular tissue is arranged in concentric layers; if lobulated, each lobule is composed of one of these concentric masses, and between

them, running from the capsule, are bands of fibrous tissue in which are found the blood-vessels.

Varieties: (1) *Liomyoma;* (2) *Rhabdomyoma.*

(1) **Liomyoma** (Non-striated).—These occur most frequently in the uterus; may occur in the prostate, esophagus, stomach, and intestines. They may become pedunculated and form polypi. They usually originate in unstriped muscle. They may be distinctly circumscribed, surrounded by fibrous capsule or ill-defined irregular masses in the midst of the muscular tissue in which they grow. Microscopically, they consist of elongated spindle-cells with rod-shaped nuclei, more or less distinctly grouped into fasciculi of various sizes; the connective tissue varies in quantity. The irregularly arranged muscular elements pass in all directions through the tumor. The few blood-vessels present are found in the connective tissue.

FIG. 123.—LIOMYOMA.—(*Gould.*)
The rod-shaped nuclei are shown in longitudinal section of the pseudo-bundles at the margin, and transverse section in the center, of the illustration.

(2) **Rhabdomyoma** (Striated).—This variety of myoma, made up of striped muscle-fiber, is exceedingly rare, and is usually congenital. It is not improbable that they are met with only as a result of the higher development of sarcomatous tissue, in which the imperfectly developed muscle remains for the most part in an embryonic stage.

Secondary Changes.—Of these the most frequent are calcareous (so-called womb-stone), fatty, myxomatous, cavernous, hemorrhagic; also inflammation (due to injury), abscess, ulceration, and necrosis. Clinically, the myomata are benign tumors.

Site.—(1) Liomyoma: Uterus (most common), esophagus, intestines, prostate, and stomach.

(2) Rhabdomyoma: In kidney, ovary, testicle, tongue, and heart.

(VI) **Neuroma.***—A *neuroma* is a tumor consisting almost entirely of nerve tissue; pure neuromata are among the rarest of new growths. The term "false neuroma" has been applied to many growths found in connection with nerves: under this head we have the fibrous, myxomatous, and gummatous tumors, found on, in or around nerves. The small multiple fibromata or neuromata of superficial nerves are usually hereditary. The amputation neuromata, which consist usually of fibrous tissue, but may contain partially regenerated nerve-fibers, form at the cut end of a nerve, in stumps after amputation, as bulbous masses, and are intimately connected with the cicatricial tissue of the stump; they are usually painful. The neuromata consist of medullated nerve-fibers; in structure they resemble the cerebrospinal nerves, from which nerves they most frequently develop. There is usually associated with the nerve-fiber more or less fibrillar connective tissue. The neuromata appear as small, hard, single nodules, and rarely attain a large size. Clinically, they are benign tumors of slow growth, and usually painful.

Varieties of neuroma: (1) *Medullary;* (2) *fasciculated;* (3) *plexiform.*

(1) **Medullary Neuroma** (*Ganglionic*).—This is a rare variety, and of little clinic importance. They contain nerve-cells, neuroglia, and vessels, and resemble the gray nerve substance in color. Virchow describes them as slightly projecting tumors in the brain and spinal marrow. They may form in the corpora striata and upon the surface of the ventricles.

* By some authorities the neuromata are classed with tumors of the epithelial type, by reason of the nervous system developing from the epiblast. The close resemblance of neuromata to connective-tissue tumors, and the absence of cancer of the nervous system, as compared with the comparative frequency of sarcoma, has led me to retain them with the connective-tissue tumors.

(2) **Fasciculated Neuroma.**—This variety is composed of nerve tubules of new formation.

(3) **Plexiform Neuroma.**—This variety consists of a series of nodules of varying size, usually small, along the course of the nerve or in a nerve plexus, the nodular masses being bound together by a varying amount of fibrous stroma.

Site.—True neuroma always originates from pre-existing nerve tissue, either from the cranial or the spinal nerves.

(VII) **Angiomata** are tumors consisting of blood-vessels bound together by a small amount of connective tissue. Some of these may be composed of newly formed blood-vessels, while others consist of more or less altered pre-existing vessels. The pure angiomata are composed of tissue entirely of new formation, but by many the tumors formed by alteration in the pre-existing vessels are included under this name.

Varieties of angioma: (1) *Simple;* (2) *cavernous;* (3) *plexiform.*

(1) **Simple Angioma** (*Simple Nevus, Telangiectoma, Birth-mark, Mother's Mark, Angioma Telangiectoides*).—This is the most common variety, and affects the skin and subcutaneous tissues. They are flat, slightly elevated, sessile tumors of a violet or dark red color, rarely bright red or pink; they are most frequently located upon the face, around the orbit, or on the neck, are usually congenital, and after birth may increase in size. On section, the vessels are thin-walled (dilated, fusiform, cylindric, sacculated, or spheric), and embedded in a fibrous or cellulo-adipose stroma. There are usually two or more large vessels which establish a communication between the nevus and an adjacent artery or vein.

Site.—Skin of the face, scalp, neck, and back. May occur on the labia, lips, tongue, and conjunctiva; rarely on the limbs. The varieties of the simple angioma are (1) *Nevus flammeus* (strawberry mark). These are of a bright red

color. (2) *Nevus vinosus*. These are dark red or port wine color, and are referred to as *port wine marks*.

(2) **Cavernous Angioma** (*Hemangioma*). — This variety differs from the simple angioma in that the vessels are less tubular. The tumor is composed of a series of irregular cavities formed by thin fibrous septa. On section, these cavities appear as irregular sinuses separated by a nucleated fibrous network of spindle-cell tissue. Many of the walls are incomplete, which shows the communication of the spaces. The cavity walls are lined with endothelium. They are spoken of as *erectile tumors*, owing to their resemblance to the erectile tissues such as the corpus cavernosum of the penis. They are rarely congenital, and may develop from pre-existing simple angioma. Usually occur early in life; rare in old age. When this form of tumor occurs in the skin and forms a livid, raised and uneven patch, it is referred to as a *nevus prominens*.

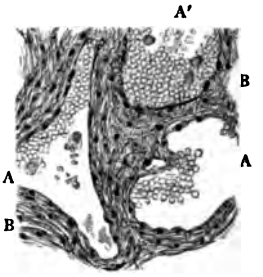


FIG. 124.—CAVERNOUS ANGIOMA.—(*Gould.*)

A, A. Caverns which during life were filled with blood, as is the upper one at A'. B, B. The fibrous walls of the caverns.

Site.—Common in the skin and subcutaneous tissue, and occasionally in the liver; may occur in the kidney, spleen, uterus, intestines, bladder, voluntary muscle, bone, mamma, tongue, larynx, subperitoneal tissue—in fact, in almost any vascular tissue.

(3) **Plexiform Angioma** (*Racemose Aneurysm, Aneurysm by Anastomosis, Cirsoid Aneurysm*).—This is not properly a neoplasm, but a pathologic alteration of the vessel. The vessels become dilated and convoluted; the dilated vessels pressing on the intervening tissue causes atrophy. The vessel walls are usually thickened. May be congenital or acquired. When occurring in the most superficial vessels it is referred

to as *nevus vasculosus* (fire mole), is congenital, and its growth may be arrested at birth. Plexiform angioma has been observed to follow injury.

Site.—Scalp (frontal and temporal region), extremities, labia pudendi, and spermatic cord.

(VIII) **Lymphangioma** is a tumor made up of dilated lymph-vessels. Rarely the dilated vessels may form distinct caverns or sacs, the *cavernous lymphangioma.* More commonly, the masses are of dilated vessels, and hence are analogous to the telangiectatic angioma already described. The tracts are the lymph-vessels, and not blood-vessels.

Site.—Lymphangioma occurs most frequently in the tongue or lip, constituting *macroglossia* and *macrocheilia* respectively.

(IX) **Lymphoma**, or tumor of the lymph-gland, covers a multitude of conditions, many of which are in no sense tumors. Thus, the glandular enlargements of tūbercle, syphilis, etc., are known as tubercular or syphilitic lymphomata. To the same group belong the inflammatory lymphomata which accompany many infections, *e. g.*, chancroidal lymphoma, suppurative lymphomata of various kinds, the glandular enlargements found in the cervical glands in various throat affections like diphtheria and scarlet fever, none of which are tumors.

Lymphosarcoma is a sarcoma of the lymph-gland, and differs but little from other forms of sarcoma except such histologic peculiarity as must arise from the site. The lymphatic enlargement which accompanies leukemia is probably an infectious process with hypertrophy and hyperplasia of the cells and stroma of the lymph-gland, or is a form of sarcoma attacking the lymph-glands: the latter view may be considered as most popular at present. Such a condition is noted in Hodgkin's disease when the hypertrophied glands are known as lymphadenomata. (See chap. VII, part III, "Lymph Glands.")

(X) **Myxoma.**—This form of tumor is composed of mucous tissue which is not, strictly speaking, an adult or physiologic

tissue ; it is, at least, the lowest grade of adult connective tissue. The tissue is identical with that which surrounds the vessels of the umbilical cord (Wharton's jelly), and resembles the vitreous humor. The tumor always contains a certain amount of fibrous stroma, and resembles an edematous fibroma. In fetal life, myxomatous tumors are met with in the subcutaneous tissues from which fatty tissue is later developed. Macroscopically, the tissue appears as a homogeneous, structureless, gelatinous mass. The majority of the cells present are angular and stellate, with long anastomosing prolongations ; others are indistinct (owing to the refractory nature of the intercellular substance), oval, spheric, or fusiform in shape. The blood-vessels are readily located, but are few in number. Usually between the cells fine elastic fibers can be demonstrated.

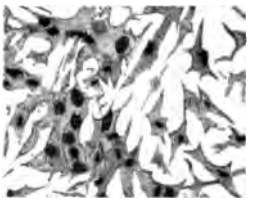


FIG. 125.—MYXOMA.

Clinically, myxoma is a peculiar, soft, gelatinous tumor, grayish or reddish-white in color, and on section yields a gelatinoid whitish albuminous or mucilaginous material. They usually occur after middle life, are of moderately slow growth, may be single or multiple (usually multiple), vary in size (not usually large), and not uncommonly recur after removal. This recurrence may not be truly a recurrence, but due to imperfect removal, after which the remaining myxomatous elements develop. Myxoma may be pedunculated or sessile ; rarely the mass is lobulated. Primarily, they are benign tumors.

Secondary Changes.—Hemorrhage (capillary) ; if extensive, may form blood cyst ; fatty ; may become inflamed, ulcerated or necrotic.

Site.—Connective tissue, most common in subcutaneous and subserous fat, submucous (nares, uterus) and intermuscular tissue ; rare from periosteum and medulla of bone, connective

tissue of organs and perineurium; they occasionally spring from the placenta (*uterine hydatids*).

EMBRYONIC CONNECTIVE-TISSUE TUMORS.

Sarcoma.

Varieties: { 1. Round-cell (small and large) 2. Spindle-cell (small and large) 3. Giant-cell (myeloid) 4. Mixed-cell 5. Alveolar } Melanotic.

The sarcomata are tumors composed of embryonic connective tissue in which the cellular constituents predominate over the intercellular substance. The embryonic cells tend to infiltrate the surrounding tissues, as a result of which sarcomata are rarely, if ever, encapsulated. If a capsule surrounds the growth, it may result from condensation of adjacent tissues, or may be a part of the tumor; in either case it is sure to be infiltrated by the tumor cells.

Histology.—All sarcomata consist of embryonic connective-tissue cells imbedded in a peculiar intercellular substance, which intercellular substance varies in amount and character. As a rule, the sarcomata contain very little true fibrous tissue, the whole mass being composed of embryonic cells; these cells are nucleated, and rarely possess a limiting membrane; the shape, size, and arrangement of the cells determines the variety of the tumor.

The cells may be mono- or polynuclear; the intercellular substance, which is usually small in amount, is closely connected with the cells, as in all connective tissues. The consistence of the tumor depends upon the character of the cell and the presence or absence of fibrous stroma. The blood-vessels are very numerous, and are usually in direct contact with the cells, or may be separated from them by a

layer of thin fibrillated tissue. The vessels lack distinct walls, the wall being composed of densely packed embryonic cells. These cells may become detached, and carried along in the current, hence *sarcoma spreads by the blood-vessels.* Owing to the thinness of its walls, hemorrhage with extravasation of the blood takes place; when this occurs the tissue becomes pigmented, and the tumor is known as *melanotic*, or this extravasated blood may become encysted (blood cyst). As a rule, the edge of the tumor is not clearly defined, there being no line of demarkation between the tumor and adjacent structures. When the tumor is of slow growth an apparent capsule may be formed of the surrounding connective tissue, due to condensation.

Clinically.—As a rule, sarcomata occur most frequently in early and middle life, but may occur at any age, and are among the most malignant of tumors. They are characterized by their tendency to extend locally, infiltrate surrounding structure, recur after removal, and to give rise to metastasis. They may be localized, at first sharply circumscribed, but are liable to become rapidly disseminated, both by local infiltration and metastasis. Secondary growths occur most frequently in the lung. The sarcomata may disseminate much more rapidly than the carcinomata.

The round-cell and large spindle-cell variety are of rapid growth and most malignant. The spindle-cell variety is much firmer, of slower growth, and less malignant. When occurring in bone, if subperiosteal, they are more malignant than when located in the center of the bone.

The following are the chief signs of malignancy in any tumor, be it sarcoma or carcinoma, but is inserted here by reason of its most appropriate applicability to the sarcomata.

(1) *Size of the Cell.*—As a rule, it may be said that the smaller the cells of a tumor the more malignant will it probably be. Thus the small round-cell sarcoma is a more malignant

tumor than that composed of giant-cells, and the small epithelial cells of a scirrhous cancer of the mamma give rise to a more malignant growth than the large, flat epithelial cells of the skin, as seen in the squamous epithelioma.

(2) *The Number of the Cells.*—If a tumor be purely cellular, the greater is the likelihood of its recurring.

(3) *Activity of the Cells.*—One of the chief diagnostic features of a malignant tumor is the tendency which its nuclei and cells have to divide; if on section a large number of the cells show mitosis in some stage of progress, the prognosis is bad, recurrence being almost assured.

(4) *Shape of the Cell.*—A small, round cell, like a lymph corpuscle, will be more readily transported by a blood-vessel or lymphatic than one which is long and tapering; hence the former will tend to reproduce the tumor in neighboring parts in preference to the latter. The round-cell sarcoma forms secondary tumors in neighboring organs, infiltrates blood-vessels, and evinces metastasis with greater readiness than one of the spindle-cell type.

(5) *The Manner in Which the Cells are Held Together.*—So far as regards the sarcomata, at least, the more loosely the cells are held together the greater the tendency for the tumor to recur. This is equivalent to saying that the more fluid the intercellular substance the more malignant the tumor. The fluidity of the intercellular substance may be partly judged by the consistency of the tumor; a soft, almost fluctuating tumor, has but little firmness in the intercellular substance.

(6) *Absence of any Tendency to Complete Their Development Intention.*—Of all signs of malignancy, this, in the case of sarcomata, is perhaps the most unequivocal. The cells do not complete the connective tissue which normally they were destined to generate. Instead of their energy being occupied in the metabolism necessary to secrete the matrix peculiar to

each, it is wholly expended in causing the cell to reproduce itself.

(7) *Tendency of the Cells to Spread into Neighboring Interfibrillar Spaces.*—In examining a tumor, the tissues round about it should be carefully investigated with a view to noticing whether its cells incline to pierce into them in long rows. If so, such a tumor is dangerous, and should be excised with a wide margin. A single cell left in the surrounding parts will reproduce it. Cancer of the mamma shows more tendency to penetrate the surrounding stroma of the gland than perhaps any other tumor. It is also one of the most malignant of tumors (Hamilton).

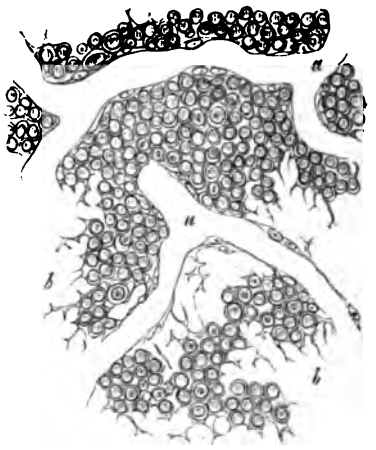


FIG. 126.—ROUND-CELL SARCOMA.—(*Rindfleisch.*) × 300 diameters.
a, *a*. Blood-vessels without distinctly formed walls. *b*. Points where the round cells have partly fallen out, showing the slight basis of reticular tissue.

(1) **Round-cell Sarcoma** (*Encephaloid* or *Medullary Sarcoma*).—This is a common variety of sarcoma, and consists of round cells with very little intercellular substance. The cells contain large, easily stained nuclei. Blood-vessels are abundant, and appear as channels or sluice-ways passing directly between the cells; there are no lymphatics present. The cells rapidly infiltrate the surrounding tissues, tend to recur after removal, and give rise to secondary deposits. The variety known as *large round-cell sarcoma* differs from the small round-cell variety in that the cells are larger and more irregular in size, and may be mono- or polynuclear; the latter resemble the giant-cell variety. The round-cell sarcoma may

occur in any tissue and at any age, even in the fetus in utero. It is a soft, rapidly growing tumor which, when on the surface, ulcerates early, and usually proves fatal in a few months.

FIG 127.—ROUND-CELL SARCOMA.—(*Gould.*)

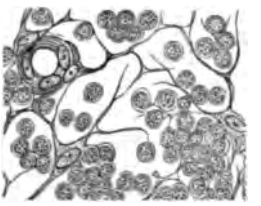


FIG. 128.—ROUND-CELL SARCOMA OF A LYMPHATIC GLAND.—(*Gould.*)

The cells have dropped out at places, showing the remainder of the intercellular trabeculæ.

(2) **Spindle-cell Sarcoma** (*Recurrent Fibroid* (Paget); *Fibroplastic Tumor* (Lebert); *Fasciculated Sarcoma*).—The spindle-cell sarcomata are the most common. They are firm in texture, and on section are translucent, and grayish or yellowish-white in color. As a rule, the spindle-cell sarcomata are much less malignant than the round-cell variety. They are divided into (*a*) small-cell, and (*b*) large-cell.

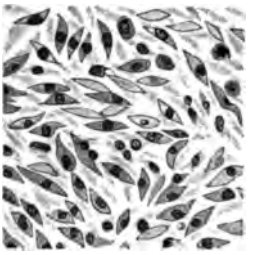


FIG. 129.—SPINDLE-CELL SARCOMA.—(*Gould.*)

(*a*) **Small Spindle-cell Sarcoma.**—This variety resembles somewhat the fibromata; the cells are fusiform in shape, with oval nuclei; there is very little intercellular substance which may be fibrillated. The bundles of cells pass in every direction. With the exception that it is firmer, grows with less speed, and does not so quickly ulcerate or prove fatal, clinically, the tumor resembles the round-cell sarcoma.

Site.—Most common in the periosteum, fasciæ, eye, antrum, breast, testicle; may occur in any connective tissue. They

tend to rapidly infiltrate the surrounding tissue and to recur locally after removal.

(*b*) **Large Spindle-cell Sarcoma.**—This differs from the small spindle-cell variety in that the cells are larger, with prominent nuclei or nucleoli, which are frequently multiple;

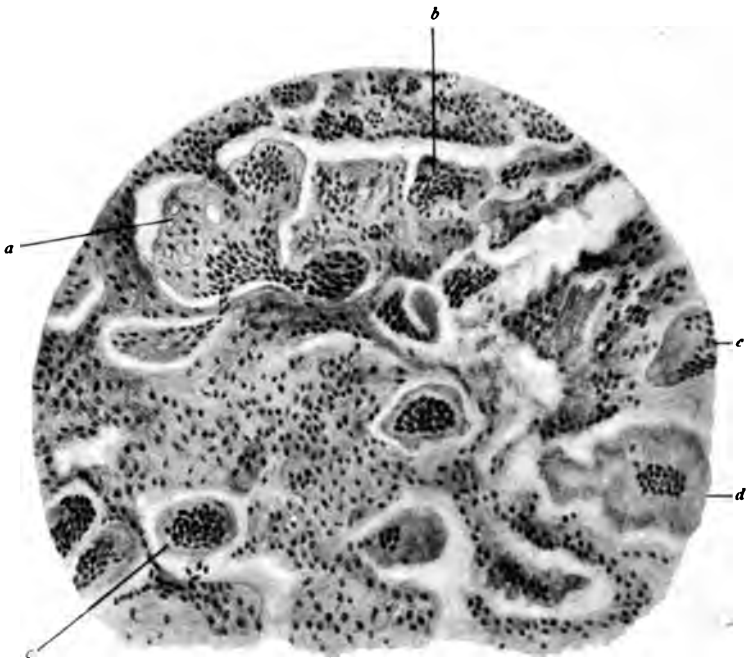


FIG. 130.- GIANT-CELL SARCOMA. (*Specimen loaned the author by Dr. Rosenberger.*)

a, *b*, *c*, *d*, *e*. Giant-cells. The larger giant-cell, *a*, shows vacuolization and dissemination of the nuclei, with pseudopod-like extension suggestive of ameboid movement. This condition is not commonly observed. The giant-cell, *c*, is more nearly typic. The admixture of other cellular elements, the usual condition noted, is well shown. ¼-inch objective, 1-inch ocular.

there is very little intercellular substance, with slight or, it may be, no fibrillation. The tumor is likely to be very soft, and is sometimes stained by extravasated blood; the growth is rapid and very malignant. They frequently become osseous (osteo

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or osteoid sarcoma), especially when occurring in the periosteum or bone.

(3) **Giant-cell Sarcoma** (*Myeloid*).—This variety resembles the spindle-cell growths, and usually occurs in connection with bone. They contain many large polynucleated cells, and often fusiform cells like those of the spindle-cell varieties. The large giant-cells are arranged almost in direct contact with the other cellular elements, there being very little intercellular substance. As a rule, the blood-vessels are not plentiful, but the tumor may become highly vascular and pulsate; they frequently become cystic. They are usually firm. They are rare after middle life, and are the least malignant of the sarcomata; they usually spring from the periosteum or endosteum. When they spring from the upper or lower alveolar processes, they constitute one variety of the *epulis*.

(4) **Mixed-cell Sarcoma.**—This variety contains round cells (large and small) and spindle cells (large and small), and otherwise resembles these two varieties.

Alveolar Sarcoma.—In this the fibrous stroma resembles that of the cancer. The nests of cells are separated by thin fibrous bands. The cells are sharply distinguished from the fibrous network, and are loosely adherent. The blood-vessels follow the course of the fibrous tissue and rarely if ever enter the cell groups. In handling the sections, should the nests of cells drop out, the remaining fibrous stroma resembles very much the transverse sections of air vesicles (alveoli). There is no variety of sarcoma so likely, under the microscope, to be mistaken for carcinoma as the alveolar sarcoma. A little experience will usually avoid this danger, particularly if the blood-vessels in the stroma be carefully studied; in the sar-

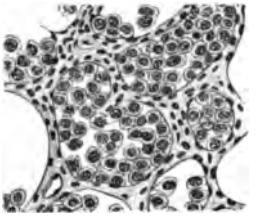


FIG. 131.—ALVEOLAR SARCOMA.—(*Gould.*)

coma many of the vessels are without walls, in the carcinomatous stroma the walls of the vessels will, in most cases, be normal, or even thicker than usual. Alveolar sarcomata are not uncommonly melanotic.

The secondary changes which a sarcoma may undergo are: Fatty degeneration, hemorrhage, cystic degeneration (blood cyst), calcification, ossification, mucoid degeneration, and pigmentation.

Site.—Round-cell Sarcoma.—Periosteum, bone, lymphatic glands, subcutaneous tissue, testicle, eye, ovary, kidney, lungs, and intermuscular septa.

Spindle-cell Sarcoma.—Subcutaneous tissue, fasciæ, intermuscular septa, periosteum, interior of bones, eye, antrum, breast, and testicle.

Giant-cell Sarcoma.—Lower and upper jaw (alveolar processes), lower end of femur, and head of tibia.

Subvarieties of Sarcoma.—**Melanotic Sarcoma** (*Melanosarcoma*).—Pigmentation may occur in any variety of sarcoma, and is usually due to hemorrhage, followed by pigmentation, due to alteration in the hemoglobin. In certain forms of sarcoma the abundance of pigment can not be fully accounted for by presuming an antecedent hemorrhage; the tumor cells seem able to elaborate pigment. These tumors may be brown or slate-colored, and in some instances almost black. Sections show the pigment in and between the cells. They are very malignant.

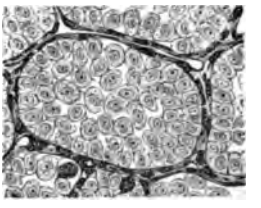


FIG. 132.—ALVEOLAR MELANOTIC SARCOMA.—(*Gould.*)

Endothelioma (*Plexiform Angiosarcoma*).—In this variety the cell nests are formed by proliferation of endothelial cells; it is highly vascular, either due to pre-existing or newly-formed vessels, which become thicker, until at length the intervascular spaces are entirely filled up. It occurs in the

subarachnoid and pia mater, and usually on serous surfaces. Occasionally, when occurring in the pia mater, the proliferated endothelial cells are aggregated into small, spheric nodules of a peculiar, shiny, pear-like appearance; it is then referred to as a *cholesteatoma*.

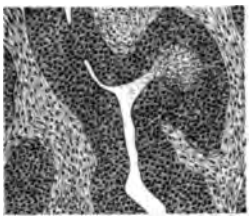


FIG. 133.—ENDOTHELIOMA.—(*Gould.*)

Psammoma (*Angiolithic Sarcoma*).—This is a peculiar tumor containing sand-like masses and originating in the brain and its membranes, more particularly in the pineal gland and the choroid plexus; it contains fine, chalky, or calcareous concretions.

Chloroma.—This is another oddly-formed cellular tumor which, on section, presents a light green or dirty brownish color. It soon fades on exposure to air. Its cause is not known. It occurs chiefly in the periosteum of the skull.

Cylindroma.—This variety is produced by partial hyaline or mucoid degeneration of a sarcoma, or when there is a combination of sarcomatous and myxomatous tissue. The term is also applied to a variety of tumors of the epithelial type, known as *cylindroma carcinomatodes*, which is characterized by the formation of peculiar homogeneous spherules within the cell nests; it is really a colloid degeneration.

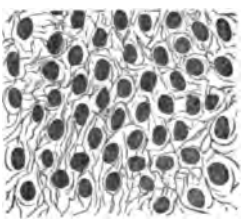


FIG. 134.—GLIOMA.—(*Gould*

Glioma (*Gluey tumors*, Virchow).—This tumor occurs in the neuroglia or connective tissue of nerve, and is a form of round-cell sarcoma; the vessels may possess lymph sheaths. Gliomata are most commonly found in the brain, spinal marrow,—both in the gray and in the white substance,—also along the cranial nerves, and in the retina.

DIAGNOSTIC FEATURES OF SARCOMA AND CARCINOMA.

	Sarcoma.	Carcinoma.
1. Origin.	Entirely mesoblastic. (Connective-tissue type.)	Epi- and hypoblastic. (Epithelial-tissue type.)
2. Stroma.	Intercellular. Rarely forms alveoli.	Vascular connective tissue, which surrounds and forms the walls of the alveoli; these communicate with one another, and contain masses of epithelial cells.
3. Cells.	Granulation tissue or embryonic connective-tissue cells; shape and size vary.	Epithelial cells contained within alveoli; shape and size vary. Distinct nuclei and nucleoli.
4. Intercellular substance.	May be present.	Absent, or merely fluid.
5. Vessels.	Embryonic in character. They are in direct contact with, or rather are composed of, the special cells, slightly modified, of which the tumor is composed.	Well developed; entirely contained within the connective-tissue stroma, and supported by the walls of the alveoli. Seldom in contact with the cells.
6. Spreads.	*Primarily* and *secondarily* by blood-vessels, rarely by the lymphatics.	*Primarily* by lymphatics, except in the later stages, when it may also spread by blood-vessels; in which case it spreads with very great rapidity. *Secondarily* by blood-vessels.
7. Pigmentation.	Frequent.	Rare.
8. Growth.	Not continuous. Likely to be interrupted.	Rapid. Continuous.
9. Site.	Primarily in deep structures; always from connective tissue.	Primarily in superficial structures or glands; always from epithelium.
10. Heredity.	Seldom hereditary.	May be hereditary.
11. Capsule.	Primarily, pseudo-capsulated; later, infiltrates the surrounding tissue.	Never capsulated.
12. Fat.	Rarely, if ever, contains fat.	Nearly always contains fat.
13. Age.	Occurs most frequently before middle life.	Most frequent after middle life.

	Sarcoma.	Carcinoma.
14. Injury.	Not uncommonly follows injury, such as traumatism.	Rarely, a history of trauma, but most commonly follows prolonged irritation. Especially is this true of the superficial forms.

MIXED TUMORS.

TUMORS COMPOSED OF BOTH TYPES OF TISSUE.—(1) **Teratoma.**—This rare variety of tumor is composed of epithelial and connective-tissue types (adult and embryonic), and originates in rudiments derived from all three layers of the blastoderm (epi-, hypo-, and mesoblastic); they are congenital tumors, usually occurring in the sacral region (coccygeal tumors), the head and neck or abdominal cavity, occasionally in the kidney.

They may be due to inclusion and imperfect development of one fetus within another, or to the abnormal development of the tissue of one fetus. They vary in size—may be small at birth, and may continue to develop or remain stationary. Dermoid cysts are sometimes classified as teratoma. (See "Dermoid Cysts.")

CYSTS.

A **cyst** consists of a connective-tissue membrane or supporting wall lined by epithelium or endothelium, and containing more or less fluid contents.

When the wall of the cyst is passive and influenced by the retained or extravasated contents in a mechanical way only, the cyst is said to be *simple* or unilocular. When several simple cysts, all arising from the same cause, in identical structure occur, they are spoken of as *multiple*. When one cyst springs from the wall of another and thus gives rise to a second or a third cyst, the process resembling proliferation, the resulting cysts are known as *proliferous* cysts; the cyst walls may be

destroyed by pressure (reciprocal), and thereby many of the cyst cavities communicate. When the cysts remain distinct, they are spoken of as *multilocular*. When the cysts communicate, they are sometimes said to be *cavernous*. When the lining membrane of the cyst develops papillomatous masses, the process is spoken of as *proliferous* or *papilliferous*.

Classified by the cause and process of development, cysts are said to be :

(1) Retention cysts. (2) Exudation cysts. (3) Cystomata. (4) Extravasation cysts. (5) Dermoid cysts. (6) Parasitic cysts.

(1) **Retention Cysts.**—These include all cysts due to blocking up of the excretory duct of a gland with accumulation of the glandular secretions. Among the most common are : sebaceous (wens) ; mucous cysts ; salivary cysts (ranula) ; milk cysts (galactocele) ; seminal cysts (true spermatocele) ; nephritic cysts ; cysts of the gall-bladder or biliary passages ; pancreatic cysts (pancreatic ranula), etc.

The wall of such cysts is composed of condensed and thickened connective tissue, and the lining cells are of epithelium. The contents are derived from the functional activity of the gland structure, altered by absorption of a part of the fluid and the degenerative changes which the cellular element of the cyst wall may have produced. Not uncommonly cysts of this class eventually contain none of the materials characteristic of the gland—*e. g.*, in hydronephrosis there may be no chemic body demonstrable as a part of the urine.

(2) **Exudation Cysts.**—These embrace cysts arising from accumulation in closed cavities ; that is, cavities not supplied by any excretory duct or analogous structure. Such cysts are typified in the accumulations in bursæ, tendon sheaths, the tunica vaginalis testis (hydrocele), canal of Nuck, etc.

The cyst wall is made up of thickened connective tissue lined with endothelium ; the sac or wall may be calcareous,

cartilaginous, fibroid, chondroid, or even osteoid. The contents are usually a clear, limpid, serum-like fluid, but may be viscid, semi-gelatinous, or contain solid bodies resulting from changes in the wall and desquamation into the cavity.

(3) **Cystoma** (hygroma or hydroma) is a cyst resembling the preceding, except that it is of new formation. The wall is of connective tissue, lined by a flattened layer of connective-tissue cells (endothelium). The contained fluid is usually clear, straw-colored, slightly albuminous, and of low specific gravity; rarely the fluid may be colored, cloudy, or even chocolate-colored. As to site, they are most frequent in the neck (hydrocele of the neck) and in the axillæ (hydrocele of the axilla); although of great rareness, they have been observed in the subcutaneous structures elsewhere,—back, belly, and even the extremities. By reason of their being most commonly congenital, occasionally associated with macroglossia, and their close resemblance to the dilated lymph-spaces of the frog, it is believed by many that they arise from dilatation of the lymph-spaces.

On two occasions I have seen cystomata of the liver; in both cases they were presumably congenital and had been mistaken for sarcomata. One of the patients died from hemorrhage into the cyst, and the other from an intercurrent malady; both were in children, aged three and six years. It is not uncommon to find these cysts cavernous, with cavities of varying sizes communicating with one another through one central space. The rule, as stated, that the specific gravity of the contained fluid is low, has occasional exceptions, as in rare instances the fluid may be as dense as the white of an egg, and so tenacious that it may not run through an ordinary cannula introduced in tapping.

(4) **Extravasation Cysts.**—This variety of cyst is formed around distended or ruptured vessels, or areas of hemorrhage, and may occur in any tissue; they include *hematocele*, or any

form of *sanguineous cyst.* The cyst wall is usually thin, and its inner surface smooth, but the reverse may be true. In rare cases the interior of the cyst—the wall—may be fasciculated. The cells lining the cavity are endothelial. Cysts occasionally occur through the extravasation of other fluids than blood; the accumulation of urine in the perineum, following rupture of the urethra, is a type of such cysts.

Site.—May occur anywhere.

(5) **Dermoid cysts** are always congenital, and arise as the result of cutaneous inclusion, or the inclusion of a blighted ovum. The wall may contain all the elements of the cutis, may be thick or thin, and not uncommonly shows a slight growth of hair; the cells lining the interior of the sac are, of course, epithelial. The contents are usually sebaceous matter and a varying amount of hair; occasionally teeth are found. When situated in the ovary, testicle, brain, eye, throat, or abdominal cavity, developing bone or cartilage may be contained within the cyst cavity; these distinctly connective-tissue products indicate the possibility of such cysts arising from fetal inclusion. The most common sites are near the orbit, root of the nose, angle of the jaw, floor of the mouth, around the sheath of the carotid vessels, near the anus, and the sacro-coccygeal region.

(6) **Parasitic Cysts.**—When any animal organism capable of surviving in the tissues gains ingress, a cyst is likely to ensue; some such parasites inevitably give rise to cysts, others not always. *Trichina*, when settled, develops a small cyst which rapidly becomes calcareous. *Coccidia* invading the liver induce a similar condition. The most important parasitic cyst in man, so far as our present knowledge goes, is the *hydatid.* This cyst arises as the result of the lodgment of the larvæ of the tænia echinococcus in the tissues. The embryo is first converted into a cyst containing a clear fluid. The wall has two layers of its own, to which is added a layer

resulting from the reaction of the surrounding elements. From the inner layer of the cyst—the endocyst—buds are developed which constitute the daughter cysts; other cysts develop in a similar way from the daughter cysts and constitute what are known as granddaughter cysts. These cysts are, therefore, proliferative. The fluid of the cyst is non-albuminous, slightly saline, clear, specific gravity less than 1010, and may contain sugar. Such cysts are likely to inflame, suppurate, or rupture, all of which terminations are unfavorable. If the parasite dies the cyst may inspissate. In the liver it is not an exceptional thing to find these inspissated cysts; the contents are usually putty-like, occasionally crumbly, and, not rarely, contain the hooklets. Inspissation represents a cure, but, unfortunately, other terminations may occur; the cyst may rupture into a closed cavity, as one of the serous cavities; rupture externally or into a bronchus or other hollow viscus occurs. A most dreaded termination is suppuration.

Site.—Liver, 46 per cent. of the cases, ovary, uterus, mamma, brain, testicle, kidney, lung, bones, muscles, serous membranes, general connective tissues. (See tænia echinococcus.)

Cysticercus Cellulosæ.—The larval form of the tænia solium induce small bladder-like cysts which may be widely distributed. In the pig, the usual intermediary host, these are about the size of a pea, and may be scattered throughout the tissues, producing a condition commonly known as "measled" or "measley" pork. In man the condition is most common in the muscles, brain, and spinal cord; occasionally the cysts may be recognized by the ophthalmologist in the chambers of the eye. (See chapter on "Animal Parasites.")

QUESTIONS.

(1) What is a neoplasm? (2) How does a tumor differ from an inflammatory enlargement? (3) How does it differ from hypertrophy? (4) Describe the proper order to be followed in studying tumor growth and describing tumors. (5) Give causes of tumors. (6) What is Muller's law? (7) What is Virchow's law? (8) Describe method of growth and extension of tumors. (9) Give clinical classification of tumors. (10) Give classification based on histogenesis. (11) Give structure of a papilloma. (12) Give forms of papilloma. (13) Give microscopic and macroscopic characteristics of each form, also site. (14) What is an adenoma? (15) Name varieties and give most frequent sites of each variety. (16) Give histology of (*a*) acinous adenoma, (*b*) tubular adenoma. (17) Give the essential histologic elements present in cancers. (18) Give general clinic characteristics of cancers. (19) Give site, gross appearance, and microscopic structure of squamous epithelioma. (20) Give same for cylindric-cell epithelioma. (21) Give same for tubulated epithelioma. (22) What are the forms of glandular cancer? (23) Give gross appearances, history of growth, and histology of hard cancer. (24) What is meant by atrophic scirrhus? (25) Give gross appearance, history of growth, and histology of soft cancer. (26) What is meant by colloid cancer? (27) What is meant by mucoid cancer? (28) How do cancers spread? (29) Why? (30) Do cancers have a capsule? (31) Name the tumors belonging to the adult connective-tissue group. (32) Give varieties of lipoma. (33) Where are fatty tumors usually located? describe the two forms and give their histology. (34) Give site, forms, structure, and characteristics of the chondroma. (35) Give forms of osteoma; give site and structure of same. (36) Give location, structure, and forms of fibroma. (37) What is molluscum fibrosum? (38) What is keloid? give site of different varieties. (39) Give forms, structure of each form, site, and degenerative changes of the myomata. (40) Give form, structure, and location of the neuromata. (41) What is an angioma? Give forms, structure, and location of each form. (42) Give same for lymphangioma. (43) What is the adult type of tissue represented by the myxoma? (44) Describe the myxoma; give its structure and history of development. (45) What name is given to all tumors composed of embryonic connective tissue? (46) How are they classified, and name the varieties. (47) At what age are sarcomata most common? (48) How do they spread? (49) What macroscopic and microscopic conditions might be of value in determining the degree of malignancy in any individual sarcoma? (50) What is the condition of the blood-vessels in sarcoma? (51) What are the physical characteristics and microscopic structure of

a round-cell sarcoma? (52) Give same for spindle-cell form. (53) Give same for giant-cell form. (54) What is meant by mixed-cell sarcoma? (55) Give the histology of the alveolar sarcoma. (56) How differentiate alveolar sarcoma from cancer? (57) What is meant by a melanotic sarcoma? (58) What is the source of the pigment? (59) What is an endothelioma? (60) What is a psammoma? (61) What is a chloroma? (62) What is a cylindroma? (63) What is a glioma? (64) Give the salient points of differentiation between the sarcomata and carcinomata. (65) What is meant by teratoma? (66) What is a cyst? (67) What is meant by a proliferous cyst? (68) What is meant by a multilocular cyst? (69) Give forms of cysts? (70) What is a retention cyst? give structure of its wall and give examples. (71) What is an exudation cyst? give structure of wall and location, also examples. (72) Give synonyms for cystoma. (73) What is the origin of cystoma, and where is it likely to be located? (74) What is an extravasation cyst and what forms its wall? Where are they usually located? (75) What is the most frequent structure of wall and contents of dermoid cysts? (76) How are dermoid cysts caused? (77) What parasites lead to the formation of cysts? (78) What are the characteristics of the cysts and the contained fluid which arise from the invasion of the tissues by the embryo of the tænia echinococcus? (79) What changes may a hydatid cyst undergo? (80) Give sites of cysts and dissemination of the cysticercus cellulosæ.

CHAPTER VII.

INFECTIOUS GRANULOMATA.

The **infectious granulomata** include a series of granulation tumors, all of which are due to some form of bacterial life, although in syphilis the precise etiologic factor has not been definitely determined. The infectious granulomata include syphilis, tuberculosis, glanders, actinomycosis, and leprosy. These are all characterized by the development of a peculiar mass formed of variously-known cellular elements arising from leukocytes and the connective tissues. The resulting tumor is known as a *granulation tumor*, as a *specific inflammatory tumor*, as an *infectious granulation tumor*, etc. The etiologic factor is found in the tumor, and, where the disease is communicable to lower animals, these granulation masses contain the cause, which, if transferred to a susceptible animal, will give rise to the disease.

SYPHILIS.

Cause.—While all the clinic and pathologic data point to the disease being due to a specific micro-organism, such has not as yet been positively demonstrated. Lustgarten has demonstrated the presence of a bacillus closely resembling the tubercle bacillus, in that it stains similarly by the anilin stains, but is more readily decolorized by acids; it is about the size of the tubercle bacillus,—if anything it is a little more slender,—and very closely resembles the smegma bacillus. As the disease is not communicable to lower animals, experimental evidence proving the pathogenic activity of the germ is not forthcoming.

Syphilis may be **acquired** or **congenital**: In the *acquired* form it is essentially a venereal disease, in that it is almost never transmitted except by sexual congress. Accidental infection does occur—*e. g.*, by kissing ; an abrasion on the hand coming in contact with infection carrying discharges, as in midwifery, may give rise to a chancre. The disease has been transmitted by vaccination, although this must now be very rare.

Congenital syphilis may be transmitted (1) by a syphilitic father; (2) by a syphilitic mother who was syphilitic prior to conception, or who acquired syphilis at the time of conception, or during gestation. Where syphilis is transmitted to the child during delivery, the condition is one of acquired syphilis.

Morbid Anatomy.—The initial lesion of syphilis consists essentially of a new growth in the skin or mucous surfaces, followed by hyaline degenerative processes which terminate in ulceration. The connective tissue of the skin is infiltrated by small round-cells, which even invade the subcutaneous structure. In these masses of small round-cells will be found epithelioid cells, and, occasionally, a few giant-cells. This converts the mass into a hard, almost inelastic, indurated area. The blood-vessels undergo sclerosis, cutting off of the blood-supply results, which may lead to liquefaction necrosis of the epithelium above ; an ulcer does not always form, liquefaction necrosis does not always occur, and occasionally a chancre will be observed in which the epithelial covering remains unbroken. When ulceration does occur, it is a cup-like or scooped-out ulcer, and is not undermined, and it is not likely to be sloughing or phagedenic. With the subsidence of cellular infiltration, repair begins ; the cells are removed, and gradually resolution is accomplished.

Associated with the initial lesion, the nearest anatomic lymphatic glands show the alterations incident to infection. The lymphoid structures proliferate. There is considerable swell-

ing, and, if the organisms of suppuration gain ingress through the ulcer, the hyperplasia may terminate in suppuration of the gland; where suppuration does not ensue, the infiltration and induration gradually subside. Following this, the lymphatic glands elsewhere (it is probable that all the lymphatic glands participate, certainly all that can be discerned from the surface) present a similar change, not, however, associated with suppuration. Syphilis has now passed into the secondary stage, and multiple cutaneous lesions occur; these are clinically important, but pathologically they are not essentially different from many skin lesions which arise independent of syphilis. Associated with the skin lesions, similar processes occur on the mucous membranes, consisting of erosions which, rarely, terminate in ulceration.

The tertiary lesions, which are pathognomonic, are the **gummata, syphilomata,** or **granulation tumors** of syphilis. Gummata are developed as masses of embryonal cells, containing lymphoid and epithelioid cells, with a very slight amount of trabeculæ; occasionally giant-cells are present; hyaline degeneration, followed by fatty changes, converts the center into a caseous-like material. The process of caseation is accompanied by syphilitic disease of the blood-vessels of the area, cutting off the nutrition to the center of the mass; after softening, the resulting material may be absorbed.

Syphilitic endarteritis consists essentially of proliferative obliterating endarteritis, due to proliferation of the intima. (For pathology of syphilis in the organs, see "Special Pathology.")

TUBERCULOSIS.

Cause.—The *bacillus of tuberculosis* is the essential etiologic factor in all the lesions of the disease. (For description of this organism see chap. VIII, part II, "Bacteriology.") Tuberculosis occurs in man and other warm-blooded animals, although a few of the latter are very rarely attacked; particularly is this

true of the horse and the ass; the tuberculosis of fowls (avian tuberculosis) is now believed to be different from the tuberculosis of man; of the races, it would seem that the Indian and negro are particularly susceptible to the disease. While there is no doubt that instances occur in which the fetus is infected in utero, and that tuberculosis can be communicated through the placenta, still such cases are extremely rare. What is inherited, and what is transmissible from generation to generation, is that peculiarity of tissue, or peculiarity of soil, which favors the development of tuberculosis; thus, it is constantly observed that tuberculosis, or this tubercular proclivity, is transmitted from parent to offspring in an almost unbroken line. Such individuals rarely escape tuberculosis, provided they have been exposed.

Other Methods of Infection.—(1) *By inoculation.* Inoculation is represented in the postmortem nodule, *verruca necrogenica* of Wilks.

(2) *Infection through the air*, as the result of inhalation of dust containing pulverized sputum laden with bacilli.

(3) *Infection through food.* This is particularly likely to occur through milk and meat, by reason of the wide zoölogic distribution of tuberculosis.

(4) The danger of infection is increased by any condition which reduces the resistance of the individual; other forms of infection; inflammation of the mucous membranes; convalescence from other diseases; bad hygienic surroundings, crowding, and similar conditions, favor the probabilities of infection.

Morbid Anatomy.—In order to secure infection the tubercle bacillus must gain access to the connective-tissue structures; as soon as this occurs, in susceptible individuals, proliferation of the fixed connective-tissue cells takes place, producing the so-called epithelioid cells of tubercle. The endothelium of the capillaries probably participates in the process of proliferation;

into this structure leukocytes wander, and invade the connective-tissue matrix, the leukocytes constituting the lymphoid cells of the tubercle. If the cellular elements be crowded, and the nutrition not abundant, the proliferated epithelioid cells may undergo incomplete segmentation, the nuclei dividing but the protoplasm of the cell remaining intact, thus giving rise to the giant-cell. It is also maintained that the packing of the epithelioid cells may lead to breaking up of the cell margins, the nuclei massing in the center, producing, thereby, a giant-cell by confluence of ordinary epithelioid elements. The

FIG. 135.—DIAGRAM OF THE STRUCTURE OF A TUBERCLE; A PURELY THEORETIC IDEA, RARELY DEMONSTRATED.—(*Gould.*)

presence or absence of giant-cells is largely dependent on the condition of crowding and the facilities afforded for complete cell division. The firm, fibrous-tissue cells of the part constitute a reticulum, or network, in which the added cellular elements just described are matted; the process, therefore, resembles an inflammatory reaction of the tissues, an attempt to limit the dissemination of the infecting agent.

The mass above described varies in size, being rarely larger than a pinhead, although it may attain several times the size; as a rule, a number of these develop conjointly and become con-

fluent; the tubercle large enough to be seen by the unaided eye contains, as a rule, many small tubercles such as that described; by the changes already noted, the capillary blood-supply is cut

FIG. 136.—CONFLUENCE OF TWO TUBERCLES. SECTION OF LUNG.

Hardened in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. The mass has originated in the vesicular wall, parts of which can be seen at *a*, *a*, *a*, running off to surround adjacent air-vesicles. *b* and *c* have been two distinct tubercles which are now beginning to show caseation. Around the caseous area is a zone of lymphoid cells in which, at *d*, is a solitary giant-cell. Such eccentrically placed giant-cells are not frequent. The vesicular walls which leave the tubercle mass at *a*, *a*, *a* show considerable thickening. (⅛-inch objective, ½-inch ocular.)

off from the center, and degenerative processes ensue; owing to the specific action of the bacillus, caseation begins; this may be accompanied by liquefaction, coagulation, or hyaline necrosis, eventually converting the mass into a yellowish

nodule of structural detritus, the so-called **yellow tubercle**; prior to the stage of softening, the mass was referred to as a **gray tubercle**; where a number of these run together the collection shows a decided tendency to evacuate itself by discharge through the most feasible route, leaving behind a cavity or ulcer. If not in all, certainly in a large percentage of the cases, the dissolution of the tubercle is brought about through a secondary infection by the organisms of suppuration. The tuberculous ulcer and abscess are more commonly, particularly in the respiratory organs, hastened to their full development by this secondary infection. This terminates the process of softening, and is an unfavorable ending of the tubercular process.

Healed-in Tuberculosis.—In favorable cases there is an attempt to limit the process by the development of a dense wall surrounding the tubercular area, through which any fluid which results from the degenerative changes may be partly absorbed, leaving behind the caseous detritus, containing not uncommonly tubercle bacilli; into the fibroid capsule, and into the caseous material, calcareous infiltration may occur, forming a stone-like mass, in which the tubercular virus may be destroyed or indefinitely stored; this constitutes the process of "healing-in," and such a mass is a **quiescent tubercle** or tubercular area, which may remain inactive or may at any time manifest recrudescence; it is, therefore, a menace, in that, under favorable conditions, the bacilli may be rapidly disseminated, giving rise to miliary tuberculosis.

Secondary Infection in Tuberculosis.—Park (Mütter lectures) lays particular stress on the mixed infections in tuberculosis; in ordinary forms of tuberculosis the symptoms are largely due to the pyogenic infection of tubercular areas; thus, a tubercular or caseous abscess may be converted into an abscess containing pus by ingress of pyogenic bacteria; where

saprophytic organisms also find lodgment, the process is likely to be attended with more marked phenomena than when the pyogenic organisms alone are present.

Site of Tuberculosis.—One of the most common sites is the lung; following this in frequency, tuberculosis of the joints, bones, and lymph-glands come next in order; these are followed by tuberculosis of the mucous membranes other than the lungs, tuberculosis of the serous membranes, tuberculosis of the spleen, tuberculosis of the liver, tuberculosis of the brain, tuberculosis of the generative organs, and tuberculosis of the heart and other muscles, in the order given.

Extension of Tuberculosis.—Tuberculosis develops as an initial lesion, inoculation, or point of primary invasion, which may extend by one of the following routes:

(1) *By the blood.* A tuberculous lymph-gland or nodule in the lung, bone, or elsewhere, may discharge its contents into a vein, and in that way we may have general dissemination of the poison; the same result may be attended by the bacilli entering the thoracic duct. It is not improbable that in the blood, as an infected embolus, the bacilli may increase in number, and eventually lodge in a capillary, or attach themselves to the vessel wall and give rise to the development of tubercle. Such dissemination is likely to be general.

(2) Another means of spread is by the *lymph-stream.* This is illustrated in the tubercular glands of the neck in children, which result from infection through the tonsils and through diseases of the teeth, gums, and oral mucosa; the same method of spread may be illustrated by the tubercular processes along the lymph-system, following tubercular ulceration of the intestine.

(3) Tuberculosis may follow the *course of other fluids:* Thus, tuberculosis of the alimentary canal may be secondary to tuberculosis of the respiratory passages, and due to the

swallowing of tubercular material ; tuberculosis of the bladder, or tubercular abscess of the perineum, may be secondary to tuberculosis of the kidney.

(4) Tuberculosis may spread by *continuity and contiguity* of tissue ; this may occur even against the ordinary course of fluid currents ; thus, tuberculosis of the ureter may be secondary to tuberculosis of the bladder, or tuberculosis of the prostate may be secondary to tuberculous processes in the rectum or other adjacent structures ; tuberculosis of the intracranial structures may be secondary to tuberculosis of the middle ear or mastoid cells, or of the frontal sinuses.

Tuberculosis of the Lymph-glands (Scrofula).—The glands most commonly involved are those of the neck, the peribronchial glands, and the intestinal and mesenteric glands ; these all point to infection through the mucous membrane, and it is most frequently found that glandular tuberculosis is associated with acute or chronic catarrhal conditions or infections of a mucosa, the lymph-stream of which drains through the glands involved.

Morbid Anatomy.—The gland is very much enlarged, swollen, and, at first, not attached to the surrounding tissues ; the gland capsule is thin and tense ; on incision, early in the case, the gland will be more or less hyaline, translucent, and very markedly swollen ; scattered throughout its structures will be shown tubercles in different stages of development and in varying degrees of degeneration ; later, these tubercles may have become fibroid, caseous, or calcareous, the gland shrunken in size and fibroid, with dense and thickened capsule ; such glands as the last described represent a " healed in " tuberculosis, or *quiescent tubercular adenitis.* In less favorable instances, the process of caseation involves the whole gland; eventually, a *peri-adenitis* is induced and the gland becomes adherent to the surrounding structures ; masses of such glands may mat together. These either break down

singly or a number caseate at once, giving rise to a tubercular abscess, the contents of which are free from pyogenic bacteria; in a small percentage of the cases pyogenic bacteria may have gained ingress either with the tubercle bacilli or as a secondary infection; under such circumstances the inflammation will give rise to more marked systemic phenomena and the suppurative processes be more active. On the whole, it may be said that tuberculosis of the glands has a tendency toward the conservative processes of sclerosis and limitation, and that general dissemination is not likely to occur; exceptions to this statement are not infrequent occurrences.

Tuberculous adenitis may be **circumscribed, limited,** or **local,** affecting a local system or a single gland; a limited tuberculosis of the glands is occasionally observed in the cervical, bronchial, and mesenteric systems. In rare instances there may be a **general** or **disseminated tuberculous adenitis.**

Tuberculosis of bone usually occurs in the neighborhood of the epiphysis of the long bone; rarely it may occur in the cancellous tissue of the short and irregular bones. König has shown that tuberculosis of bone arises as a result of a tubercular infarct, and Müller produced such a process by the intravascular injection of tubercle bacilli. Developing near the epiphysis, the tubercular process tends to limitation and caseation; occasionally, however, it may be disseminated through the entire length of the bone, closely resembling osteomyelitis, and in such cases the entire shaft may undergo necrosis; more commonly, however, the epiphysis alone is involved; this may be limited to a single tubercular collection in the interior; the tubercular masses may be multiple, or, eventually, the entire epiphysis may undergo necrosis, or the tubercular process may penetrate the joint. As the result of injury, surgical operation, or otherwise, there is a great tendency to the general dissemination of tuberculosis from primary caseous masses in bones or joints; hence operations

on tubercular bones should be complete, or should not be attempted. Where the periosteum gives way, or where the tubercular process extends to the surrounding soft parts, a tubercular abscess is engendered—a phenomenon observed in tuberculosis of the bodies of the vertebræ.

Tuberculosis of the Joints.—This results, in a large number of cases, from extension from the bone ; it may begin as tuberculosis of the bone, cartilage, synovia, or ligaments; there is developed a granulation tumor, which undergoes caseation and softening ; the articular surface of the bone is denuded, and where the ligaments are attached the periosteum is loosened, and the tubercular process extends to the peri-articular tissues. Very closely allied to tuberculosis of the joints is tuberculosis of the tendon sheaths ; this is occasionally observed at the wrist, the ankle-joint, and wherever extended serous surfaces are associated with tendons.

Tuberculosis of the Lung.—Tuberculosis of the lung arises clinically as (1) an *acute miliary* process, *acute phthisis, tuberculopneumonic phthisis*, or *galloping consumption ;* (2) as *chronic ulceration* or *ulcerative phthisis*, or *caseous tuberculosis*, and (3) as *fibroid phthisis*. These represent but different stages or different degrees of infection in the individual, or different degrees of resistance.

Mode of Infection.—(1) Pulmonary infection may occur through the air-passages as a primary infection, such as might follow the inhalation of dust containing tubercle bacilli, or a secondary infection such as would result from the aspiration into the lung of caseous material from a broken-down bronchial gland, tracheal or laryngeal ulcer ; (2) infection may occur through the blood- or lymph-streams ; as either of these conducts the bacilli directly into the intervesicular connective tissue, the resulting tubercular processes are identical.

When the bacilli are deposited in the connective tissue of the lung, tubercles develop in that structure, and the extent

of the tubercular invasion is, of course, dependent upon the purely local or more general dissemination of the poison and upon the resistance of the tissues; associated with the

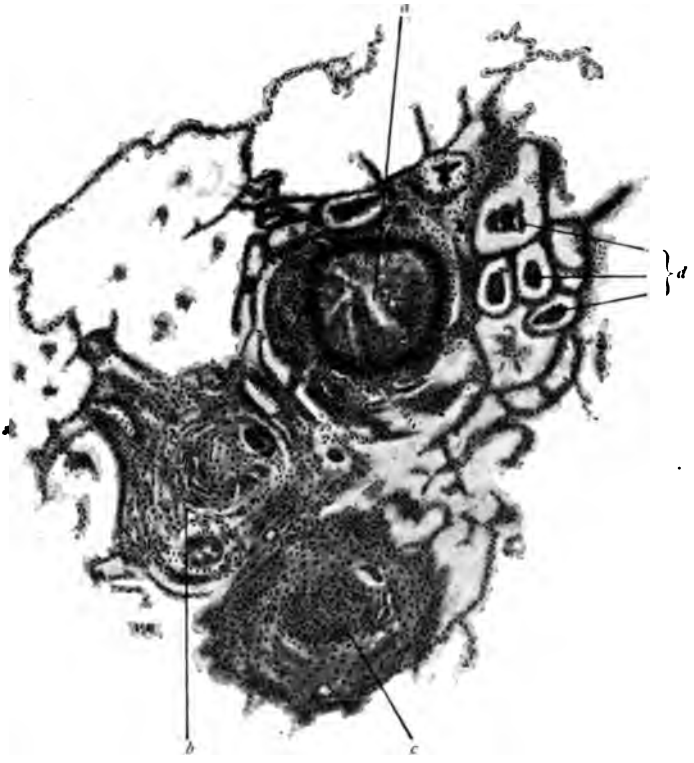


FIG. 137.—TUBERCULOSIS OF THE LUNG.

Tissue fixed in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. *a*. Tubercle with advanced caseation. *b* and *c*. Tubercles with less advanced degenerative changes. In the upper and right quadrant of *b* is seen a giant-cell. *d*. Three air-vesicles partially filled by inflammatory products, tubercular pneumonia. (¼-inch objective, 1-inch ocular.)

development of the tubercle there is inflammation of the epithelial lining of the air-vesicles, constituting either a true pneumonia or bronchopneumonia, so that a lobe, or a lung,

or rarely both lungs, may represent some form of bronchopneumonia, or what very closely resembles a lobar pneumonia, *tubercular pneumonia;* as a result of desquamation of the epithelial-cells from the air-vesicles, much of the lung tissue may be so occupied by the products of inflammation that it may be solid. This constitutes what is clinically known as *acute pneumonic phthisis*, or galloping consumption. The changes which

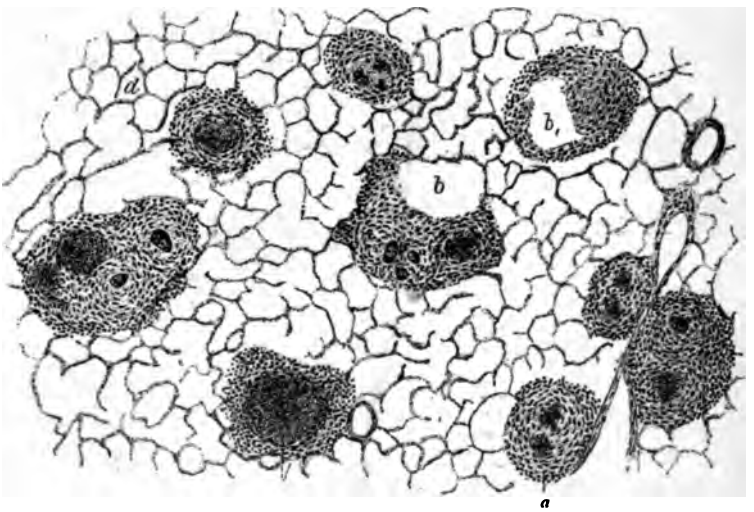


FIG. 138.—ACUTE DISSEMINATED TUBERCULOSIS OF THE LUNG. NINE AREAS OF AGMINATED TUBERCLES ARE SHOWN.—(*Schmaus.*) × 40 diameters.

a. Tubercle undergoing caseation. *b*. Group of at least four tubercles; in the two to the right giant-cells are still visible, while the two to the left and above are showing central softening. *d*. Alveolus.

the tubercles undergo are those already described. When the area of infection is small, the tissue resistance marked, when caseation is limited and the tendency is toward repair, rather than destruction of tissue, and where there are extensive fibroid changes in the area involved, the condition is referred to clinically as **fibroid phthisis.**

When the infection reaches the lung through the air-

passages the morbid processes differ. There may have been an extensive bronchopneumonia, and this is the most common history; if such a bronchopneumonia has not been present, one certainly develops with the lodgment of the tubercle bacilli; from the mucous membrane of the lobule desquamation occurs, and a more or less marked bronchopneumonia, with an accumulation of the inflammatory products occupying either few or many lobules of the lung structures, occurs. From the specific action of the tubercle bacilli, instead of resolution, caseation of these areas of tubercular

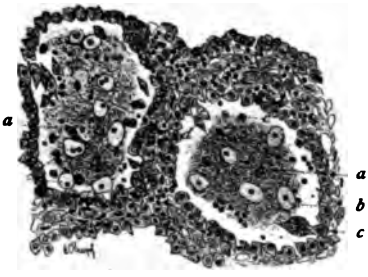


FIG. 139.—TUBERCULAR PNEUMONIA. THE DESQUAMATIVE LESION WITHIN THE AIR-VESICLES, WHICH OCCURS NEAR TO AND AROUND TUBERCLES IN THE LUNG.—(*Schmaus.*) × 250 diameters.

a, *a*. Exudate undergoing degenerative changes in the air-vesicle. *b*. Round-cells in same. *c*. Desquamating cells. The intervesicular walls are thickened.

bronchopneumonia occurs; the vesicular structure is involved in the process of caseation. With the breaking down of the intervesicular walls the connective tissue of the lung is exposed; in individuals whose resistance is good, sclerosis and limitation of the tubercular process occurs; in others, with the breaking down of the intervesicular wall and opening of the lymphatics a more or less marked dissemination takes place; once this is established the picture does not differ from tubercular processes associated with infection through the lymph- or blood-stream; the damage done, under such conditions, may be limited, restricted tubercles or caseous nodules scat-

tered throughout the lung or limited to one or two localities; or a most extensive and widely-diffused tuberculosis may be secondary to the initial infection in the bronchopneumonic area.

Cavity Formation.—A mass of tubercles occurring in one area become confluent, with tubercular pneumonia of the

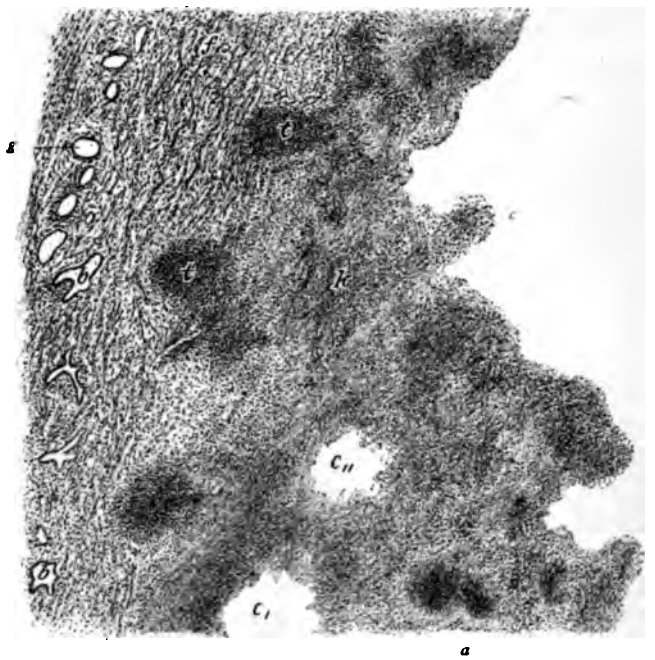


FIG. 140.—WALL OF A TUBERCULOUS CAVITY.—(*Schmaus.*) × 100 diameters.

c. Cavity. *c'*, *c''*. Smaller cavities which will, eventually, as the result of caseation and liquefaction of the intervening tissue, blend with the larger cavity. *b*. Remains of a bronchus. *t*, *t*. Tubercles undergoing softening. Just over *a* is shown other tubercles. *k*. Caseous wall. *g*. Blood-vessel.

intervening vesicular spaces, producing a solidified area in the lung. The obliterative changes in the vessels, to the part involved, cut off the nutrition, and degenerative phenomena, coagulation necrosis, and eventually caseation, convert the area into what practically constitutes a tubercular abscess.

Mixed or secondary infection (see p. 225) has much to do with the changes in the tubercular mass. By extension into adjacent tissues a bronchus is reached, its wall softened and eventually destroyed, thereby emptying the degenerated, caseous, or semifluid contents of the tubercular area into the bronchus, from which it is removed by expectoration; some of the infective material may be inspirated into other parts of the lung, inducing new areas of infection.

The wall of such a cavity, formed as just described, is lined by a layer, varying in thickness, composed of necrotic and caseating tissue containing tubercles in all stages of softening. If, as is rare, the process has been simple up to this point, secondary infection is now assured; molds, yeasts, and various saprophytic organisms, as well as pyogenic bacteria, gain ingress, hastening the dissolution of the caseous material which surrounds the cavity. External to the caseous layer is a wall of granulation tissue and lymphoid elements which usually contain tubercles. The air-vesicles show tubercular pneumonia, and in many cases there is an increase in the fibrous tissue of the interalveolar walls for some distance beyond the truly tubercular mass.

In very rare cases these large tubercular collections discharge through the chest wall rather than into a bronchus. The writer has observed one such case. The cavity is not uncommonly traversed by blood-vessels or bronchi, the tissues of which, having resisted the tuberculous process, are not fully destroyed. In the above form the condition is spoken of as **caseous** or **ulcerative tuberculosis** or **phthisis.**

Tuberculosis of the Serous Membranes.—Infection here may occur through the blood-stream, through the lymphatics, or by contiguity, as in tubercular middle-ear disease; it may be associated with a distinct outbreak, of a serofibrinous inflammation; in the fibrinous mass, lying immediately adjacent to or in the serous surface, will be found many miliary

tubercles. Occasionally tuberculosis of a serous membrane may occur without any distinct serofibrinous or hemorrhagic exudate into the cavity ; under such circumstances the tubercles are large, and are more in the connective tissue beneath the membrane than in the serous membrane proper. Such tubercular processes are most likely to be observed in the peritoneum ; there may be considerable serum in the cavity without the usual

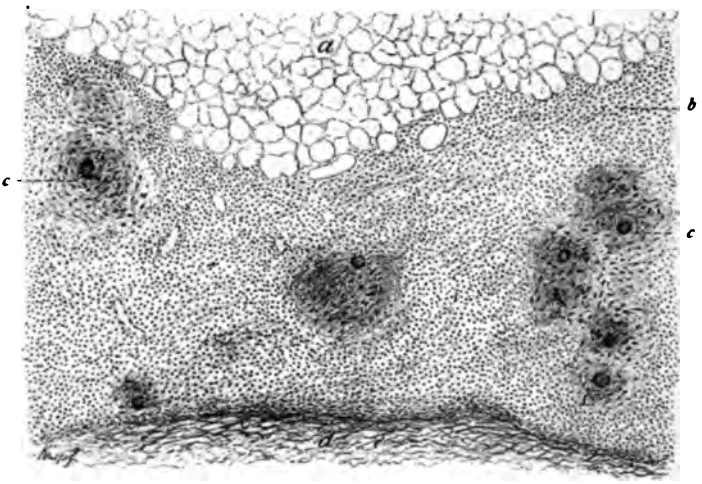


FIG. 141.—ACUTE TUBERCULOSIS, VERTICAL SECTION OF SEROUS MEMBRANE AND INFLAMMATORY EXUDATE.—(*Schmaus.*) × 250 diameters.

a. Subepicardial fat. *b*. Layer of granulation tissue which extends to the layer of fibrin *d*. *c*, *c*. Tubercles containing giant-cells. Other tubercles are shown, in some of which degenerative changes are beginning to evince themselves.

evidence of marked inflammation. In the serous membranes the tubercles can be readily recognized, and by selecting a thin portion and examining it by transmitted light the tubercles will be, as a rule, distinctly seen. The serous membranes most commonly involved are the pericardium, pleuræ, peritoneum, the serous covering of the brain, cord, and tendon-sheaths. (See "Inflammation of Serous Membranes.")

For the pathology of tuberculosis of mucous membranes,

the alimentary canal, genito-urinary organs, etc., see special pathology of those structures.

Tuberculosis of the Skin.—This constitutes what is spoken of as lupus. **Lupus** usually begins as a few small vascular nodules, in which the tubercles occur in the subcutaneous or in the connective tissues of the skin; where the nodule ulcerates, the condition is spoken of as *lupus exedens;* where there is no tendency toward ulceration, but where cicatrization occurs, the condition is spoken of as *lupus non-exedens.* In the tuberculous nodules, situated in the skin, the tubercle bacillus can be demonstrated; the process is usually very chronic and intractable.

GLANDERS.

Glanders is a bacterial disease occurring in horses and asses, but communicable to man, and is due to the *bacillus mallei.* (For description of bacillus see chapter VIII, "Bacteriology.") Glanders in man occurs in two forms: (1) *Localized, circumscribed,* or *chronic glanders* or *farcy;* (2) *General, disseminated, acute,* or *septicemic glanders.*

(1) **Localized Glanders.**—When glanders affects the skin and adjacent lymph-glands, it is spoken of as *farcy;* when the mucous membranes are affected, the condition is spoken of as *glanders;* so that at one time it was customary to speak of acute and chronic glanders, and acute and chronic farcy. It is now recognized that glanders and farcy are due to the same cause, and there is little essential difference between the pathology of the "farcy bud" and the glanders nodule.

It does not seem probable that the organism can gain ingress except through an abraded or wounded surface. As communicated to man, the disease usually comes from the horse, and is therefore most common in hostlers and those employed around stables, etc. When the glanders bacilli localize in the subcutaneous or submucous tissue, there

develop small nodules, rarely as large as a pea, made up of an almost pure round-cell infiltrate, containing a few giant-cells and the characteristic bacilli. By necrosis, the mucous membrane or the skin breaks down, and the resulting ulcer is usually foul, without any abundant discharge; where a number of the ulcers are located near one another, they not uncommonly show a decided disposition to become confluent. There is likely to be lymphangitis, extending to the neighboring lymph-glands, which may become large and suppurate. This constitutes the so-called **chronic glanders** or **chronic farcy.**

(2) **Acute Glanders.**—In the acute form, the condition more closely resembles miliary tuberculosis in the rapid dissemination of the poison and the wide-spread distribution of the lesions. Weichselbaum describes a case of acute glanders, in which, without any apparent initial lesion, there occurred multiple glanders nodules throughout the viscera which were not diagnosticated during life; at the postmortem, a thrombus was found in one of the meningeal veins, and from this, no doubt, had arisen infected emboli, which had given rise to the general dissemination of the lesion. In this condition the bacilli are found in the blood and in many of the discharges; there are likely to be multiple cutaneous eruptions, with implication of the larger joints, as in other forms of septicemia; in the male the testicles may be involved. Multiple abscesses may occur throughout the body, closely resembling pyemia. Death usually occurs from exhaustion. This constitutes the septicemic form of glanders, and may occur (1) without any initial lesion which can be discerned; (2) it may be associated with an initial lesion which runs a rapid course; (3) it may terminate the chronic form of farcy or glanders already described.

ACTINOMYCOSIS.

Actinomycosis is a disease most common in the cow, where it is known as *clyers*, *wooden-tongue*, *big-jaw*, etc. The disease is due to the ray fungus, for description of which see chapter on "Bacteriology." The fungus, in masses, is usually sufficiently large to be recognized in the discharges as small yellowish-white, white, or brownish-white tufts, varying in size from a grain of sand to a pin's head; these, if picked out of the discharge and crushed between cover-glasses, may be stained and demonstrated as elsewhere described. The infection usually occurs through the mouth and pharynx, probably through some abrasion in the mucous membrane, or possibly through a diseased tooth. Chiari first described a case in which the primary infection was probably a mural implantation on the intestinal wall.

Morbid Anatomy.—Once the fungus secures admission to the connective tissues, there is engendered a granulation tumor containing large masses of small round-cells, a few epithelioid elements, and giant-cells very closely resembling in structure a tubercle; the lessened tendency to necrosis or caseation, however, permits these masses to accumulate and become of considerable size, when, prior to the discovery of the cause, they were not uncommonly mistaken for sarcomata. Probably on account of the large size of the germ, dissemination by the lymph-stream is less common than by the blood-supply. The actinomycotic nodules are prone to break down into material resembling pus; whether this pus formation could occur independent of pyogenic organisms was for a long time a disputed point, but it is now generally admitted that actinomycosis may terminate in suppuration, resulting from the direct action of the fungus independent of other organisms.

Sites.—The skin, teeth, tongue, jaws, stomach, and intestines. It has been observed in the generative organs, particu-

larly in the Fallopian tube; the disease also occurs in the medulla of long bones and in the cancellous tissue of small bones, and has been described in the mastoid cells and in the middle ear. Primary pulmonary actinomycosis has been observed; primary cerebral actinomycosis occurs, although cerebral actinomycosis is usually due to metastasis, the fungus reaching the brain after a local lesion elsewhere.

LEPROSY.

Leprosy is a feebly contagious and highly malignant disease, due to the *bacillus lepræ*. The disease is probably propagated largely by inoculation in susceptible individuals, and manifests itself in two forms,—(1) **anesthetic leprosy,** and (2) **tubercular leprosy.**

(1) **Anesthetic leprosy** involves the nerves, skin, bones, and viscera. The nerves most commonly affected are ulnar, median, radial, musculospiral, intercostohumeral, external cutaneous, and perineal. The nerve affected is red, swollen, rounded in shape; later it becomes harder, pale and grayish in color, with nodular enlargements. Microscopically, the neurilemma may or may not be changed; in most cases, however, it becomes thickened, fibrous, and infiltrated with granule cells (leprous cells, lymphoid cells). Cicatrization and contraction may obliterate the function of the diseased nerve. Occasionally the central nervous system shows some edema, and there may be an excess of fluid in the ventricles and the subarachnoid space. The larger nerve-trunks are likely to show some fibroid hyperplasia, with slight atrophy; the cutaneous nerves are degenerated, hence the skin is anesthetic; the hair-bulbs, the sweat-glands, and the sebaceous glands are atrophied and fibroid. Necrosis and caries of the long bones have been observed.

(2) **Tubercular Leprosy.**—With infection of the skin or mucous membranes, sometimes preceded by the so-called

prodromal eruptions, typical leprous tubercles are developed; "they may be flat or prominent, oblong or round, isolated or confluent, and in color varying from pale violet to a dark brown; . . . they are generally soft, but may be hard" (Danielssen and Boeck, quoted by Sommer). These tubercles occur anywhere on the body, with the exception of the scalp; they are also rare in the palms of the hands and soles of the feet. Microscopically, each tubercle is made up of granulomatous tissue, composed of small, round lymphoid and epithelioid cells retained in the loose connective-tissue matrix; in these masses the bacilli abound, both between and in the cells. Liquefaction necrosis occurs, followed by infection with pyogenic organisms, terminating in ulceration; such ulcers often heal rapidly, or by extension may lead to extensive sloughing; the nodules occur also on the mucous membranes, particularly of the nose and larynx. The bacilli may involve the viscera, lung, liver, spleen, and kidneys, in which they occasionally give rise to leprous nodules.

Mixed forms of leprosy are not uncommonly seen, both the anesthetic and tubercular type being present. In other cases an attack of the anesthetic form terminates in the tubercular, or the tubercular type develops evidences of extensive anesthesia.

QUESTIONS.

(1) Give synonyms for infectious granuloma. (2) Name the infectious granulomata. (3) What is the supposed cause of syphilis? (4) What are the forms of syphilis? (5) Give morbid anatomy of the initial lesion of syphilis. (6) Give morbid anatomy and histology of a gumma. (7) What is the cause of tuberculosis? (8) How explain the apparent heredity of tuberculosis? (9) Give methods by which infection may occur. (10) Give the minute anatomy of a tubercle, the sources from which its cellular constituents arise, and their arrangement. (11) How are giant-cells formed? (12) Describe the gross characteristics of a tubercle; (*a*) gray tubercle, (*b*) yellow tubercle. (13) What is meant by a "healed-in tubercle"?

(14) Describe its formation. (15) What is meant by secondary infection in tuberculosis, and what is its effect? (16) Give sites of tubercles. (17) How may tuberculosis spread? (18) What lymphatic glands are most commonly tubercular, and what is the most frequent point of ingress of the infection? (19) Describe a tubercular gland. (20) Describe the different degrees of tubercular adenitis, and give the termination. (21) What is meant by peri-adenitis? (22) What is meant by a local tubercular adenitis? and give synonyms. (23) What is meant by general tubercular adenitis? and give synonyms. (24) Where is the most frequent location of tuberculosis in bone? (25) How does the process develop, and what are its terminations? (26) Under what conditions may a local tubercular lesion in bone give rise to general tuberculosis? (27) In what structures of a joint may tuberculosis arise, and what is its usual course? (28) In what form does pulmonary tuberculosis occur? (29) How may infection reach the lung? (30) Describe the lung of acute miliary tuberculosis. (31) Describe a lung of fibroid phthisis. (32) Describe a lung of ulcerative phthisis. (33) What is the usual source of infection in tuberculosis of serous membrane? (34) Describe a serous membrane, showing miliary tuberculosis. (35) What serous membranes are most prone to tuberculosis? (36) Describe a tubercular ulcer of a mucous membrane. (37) What tubercular processes may occur in the genito-urinary organs? (38) What are the forms of tuberculosis of the skin, and what is the essential histology? (39) What is glanders? (40) What are the forms of glanders? (41) What is localized glanders, and what are the synonyms? (42) What is the difference between glanders and farcy? (43) What is the most common source of infection? (44) Describe the nodule of glanders, and the changes it may undergo. (45) Under what conditions may septicemic glanders occur, and how does it differ from localized glanders? (46) What is actinomycosis? and give synonyms. (47) To what is it due? (48) How would you recognize the fungus, and what are its peculiarities? (49) How does infection usually occur? (50) Give the histology of an actinomycotic nodule. (51) How does actinomycosis usually disseminate? (52) Is the actinomyces fungus pyogenic? (53) In what organs is the germ likely to localize? (54) Give forms of leprosy. (55) In anesthetic leprosy what tissues are involved, and what changes do they undergo? (56) Describe the tubercle of tuberculous leprosy and give its histology. (57) What changes may the leprous tubercle undergo?

CHAPTER VIII.

BACTERIOLOGY.

BACTERIOLOGIC TECHNIC.

In order to study bacteria we must cultivate them and obtain them in pure culture, a term to be explained later. In order to successfully cultivate germs we must secure a soil upon which they will grow. Such a soil is called a *culture medium*. The soils, or culture media, are classed under two heads,—the **natural** and the **artificial**; of each of these we have two kinds, the *fluid* and the *solid*.

Natural Culture Media.—*Fluid.*—Blood-serum, milk, urine, aqua coca, hydrocele fluid, eggs or egg-albumen, etc. *Solid.*—Blood-serum, eggs, potatoes and other tubers, and fruits.

Blood-serum is the most valuable of all natural culture media, and may be used either in the fluid or solid state. The serum may be obtained from any of the lower animals, though that of the calf or ox is to be preferred. The blood is collected in sterile jars at the time of slaughtering. If the blood is passed directly from an artery into a sterilized jar it will remain sterile. The freshly-drawn blood is allowed to coagulate in the sterile receiver; it is then removed to the laboratory. A sterile glass rod is passed around the outside of the clot, between the clot and the jar, in order to detach the fibrin from the jar that the clot may contract. The jar is then placed on ice. In from twelve to twenty-four hours the clot will have separated, and the serum may be siphoned off with a sterile siphon. If it is clear it may at once be filled into tubes; if there be much suspended coloring-matter—red

blood-cells—it had best be set in the ice-box for these to precipitate, after which it may be filled into the culture containers. If this operation be conducted with proper care, the serum will not require sterilization, and may be used in its fluid state. If, however, a solid medium is wanted, the serum is sterilized and "set" by heating.

In order to sterilize blood-serum it must be heated one hour each day for four days; as high temperatures cause coagulation of the albumin, the heat had best not exceed 65° C. If it is desired to use it as a solid medium, the conversion from a liquid to a solid medium is accomplished by gradually raising the temperature, until coagulation is just sufficient to render the serum solid; at this stage it is slightly opalescent, of a yellowish straw color, and easily penetrated by a needle. The temperature necessary for solidification rarely exceeds 70° C. Sterilization may be accomplished at 100° C., in which case the serum is white, like coagulated egg-albumen. There is no reason to believe that it is less efficient for culture purposes.

Löffler's blood-serum mixture contains:

Bouillon, containing one per cent. glucose,	1 part
Blood-serum,	3 parts.

The two are mixed, filled into the tubes, and sterilized as directed for blood-serum. The medium is especially useful for the bacillus diphtheriæ.

Milk is a very useful culture medium. It is used either alkaline, neutral, or acid, and, with the addition of an indicator, for testing the reaction of growing cultures. Test-tubes, charged with the desired quantity of skimmed milk (all the fat should be removed), are thoroughly sterilized by exposure to steam. Certain bacteria may be identified by their peculiar action upon milk. Thus, some organisms induce coagulation of the casein, while others peptonize it; some develop an alkaline reaction, others an acid.

While they are useful, the employment of urine, aqua coca, and hydrocele fluid is not general.

Boiled potato affords us a splendid culture medium for the growth of many bacteria. Potato used as a culture medium is first thoroughly washed in water to remove dirt, then washed in a 1 : 1000 solution of corrosive sublimate, followed by sterilized water for ten or fifteen minutes to remove the mercury. It is then cut into slices. With an apple-corer cut from the slices pieces of the proper size, slip them into sterilized test-tubes, and add a small quantity of distilled water to prevent rapid drying after sterilization. They are now ready to be sterilized, which may be accomplished by placing them in an autoclave for from twenty to twenty-five minutes; or, by fractional sterilization, an hour a day, for from three to five days, in a steam sterilizer. They are now ready for inoculation.

FIG. 142.—MOIST CHAMBER FOR POTATO CULTURE.

To use this dish or any similar chamber for potato cultures, the dish is sterilized in a hot-air sterilizer and allowed to cool. In the bottom is placed a blotter, moistened with a 1 : 1000 solution of corrosive sublimate. The potato is cleaned as described in the text, and sterilized whole; a thin knife, such as is figured on page 30, is also sterilized; the worker thoroughly disinfects his hands, takes the sterile potato in the left hand and the sterile knife in the right hand; the potato is then incised in its longest diameter, and, without separating the two halves, an assistant raises the upper half of the dish by the knob while the potato is quickly placed on the sterile blotter and the two halves separated so that the freshly-incised surface of each half is turned upward; the lid is now quickly replaced. If no growth occurs on the potato in three or four days, it may be considered sterile, and be inoculated.

Sterilized eggs are occasionally used for the cultivation of anaërobic bacteria. The eggs are thoroughly sterilized as for blood-serum, a point in the shell carefully penetrated with a sterile borer, the egg inoculated, and sealed with wax. Occasionally sterilization may not be necessary, but without it incubation can not well be applied, as the chick develops too rapidly. After inoculation the egg may be dipped in hot paraffin, which, on cooling, forms an air-tight covering.

Artificial Culture Media.—*Fluid.*—Inorganic solutions, organic mixtures, bouillon, and vegetable and animal infusions. *Solid.*—Bouillon, milk, etc., solidified by the addition of gelatin, agar-agar, or gelatin and agar-agar. To cultivate certain bacteria,—the tubercle bacillus, for instance,—it may be necessary to add glycerin to the medium.

The most useful artificial culture media are infusions of beef

FIG. 143.—INSTRUMENT FOR CUTTING PLUGS OF POTATO FOR POTATO CULTURES. The cut plugs are washed in water and pushed down into test-tubes into which the potato segment fits closely. A little water is added to just come up to the lower end of the plug. The tubes are then sterilized as directed in the text.

and mutton containing a small quantity of peptone. Most of the bacteria develop quite readily in such media. The stock culture medium is Koch's **alkaline-beef-peptone bouillon.** For ease and rapidity of preparation the following is recommended: Take an ordinary farina boiler (agate-ware is best), and fill the outside kettle with sufficient water to well inclose the inside can; into the latter put one liter of water, which

had best be distilled; with a diamond or file, mark on the side of the can the height of the fluid. Obtain 0.5 of a kilogram of finely-chopped lean beef from which the fat has been carefully removed; add this to the water, a little at a time, stirring constantly so as to assure every piece of the meat being well penetrated. When mixed this forms an almost blood-red fluid, which at one time was thought must stand on ice twelve hours before proceeding with the next step. We do not now, commonly, find this necessary, although some workers apparently always macerate for the twelve or twenty-four hours, as originally advised. Whether we macerate or not, the next step is to add the peptone and salt. Take ten gm. of Witte's dried beef-peptone and five gm. of salt (sodium chlorid) and mix them thoroughly in a mortar or teacup; add just enough water to rub the mixed powders into a thin paste, which is now added to the meat-and-water mixture in the farina kettle and thoroughly stirred into the mass. The water in the outside kettle is now brought to a boil, during which time the mixture in the inside kettle has been frequently stirred. As soon as the albumin begins to coagulate the stirring is stopped, and when it is fairly advanced, after fifteen or twenty minutes' boiling, the inside kettle is removed from its surrounding water-bath and its contents brought to a boil over the flame, care being used that it does not boil over. The meat will collect with the coagulated albumin into a rather dense mass, which should be broken up, so that the interior may be fully penetrated by the boiling fluid in order to fully extract the salts contained in the meat.

FIG. 144.—AGATE-WARE WATER-BATH (FARINA KETTLE).

Used in making culture media, and convenient for many purposes about the laboratory; the capacity should be about 1000 c.c. for inside boiler.

After thirty minutes' boiling the mass is removed from the flame and strained through flannel. The water lost by evaporation must be made up by pouring over the meat in the strainer enough cold water to bring the filtrate to one liter. If any fat is seen over the surface of the fluid, as much as possible is removed with a spoon or by gently touching it with paper or a clean cloth. The filtrate will usually be clear, and, if not, it must be filtered. Tested with an indicator, this fluid will be found acid, and must be made neutral or faintly alkaline. This is best done by adding, drop by drop, a ten per cent. solution of caustic soda (sodium hydroxid). The best indicator is a phenolphthalein solution, made by dissolving one gm. of phenolphthalein in 1000 c.c. of 50 per cent. alcohol. A watch-glass containing about one c.c. of this solution is placed conveniently, and into this a drop of the bouillon is mixed, a fresh watch-glass being used for each drop; as soon as alkalinity is reached, the indicator turns a bright rose color, which, while distinct, should be faint. Litmus paper may be used instead of the above, but is less delicate, although for all ordinary purposes it is sufficiently accurate. As a rule, the alkalinity can be told by the bouillon becoming faintly cloudy, the salts and albumins, insoluble in an alkaline fluid, precipitating. To complete the formation of this precipitate the fluid is thoroughly boiled for at least thirty minutes, and then filtered. It is advisable, where a perfectly clear fluid is absolutely essential, to cool the medium, filter, re-boil, and again filter; this is rarely done, and is useless except that it assures the medium remaining clear; after each boiling, and before finally filling the culture vessels, its alkalinity must be tested, for, in some unexplainable manner, a fluid previously

FIG. 145.—AGATE-WARE FUNNEL FOR FILTERING HOT FLUIDS.

Agate-ware has almost exclusively superseded any other ware in the preparation of culture media.

known to have been neutral, or even alkaline, may become acid. When finished, the above product is known as neutral-, alkaline-, or acid-beef-peptone bouillon, the first word of the name always indicating the reaction. When intended for the cultivation of tubercle bacilli, glycerol (glycerin) is added (the amount commonly employed is six per cent.),—60 gm. of the glycerol, which must be weighed and not measured, to 1000 c.c. of the bouillon. It is now known as alkaline-glycerin-beef-peptone bouillon.

Instead of the 0.5 of a kilogram of beef used in the above, two gm. of meat extract (Liebig's or Armour's) may be substituted. The preparation is practically the same, except, of course, the flannel filter is not needed, and, as the meat salts are exceedingly difficult to remove, filtering while hot, and again when cold, may have to be frequently repeated to secure a perfectly clear fluid.

When it is desired to render the above solid, gelatin or agar, or both combined, may be used.

Beef-peptone-gelatin.—To 1000 c.c. of cold bouillon, 100 gm. of gelatin ("gold-leaf," in sheets), torn or cut into fragments, are added and allowed to soak for fifteen or twenty minutes, until the gelatin swells up and becomes flaccid; it is then easily dissolved by gently heating in a water-bath; by the time it has reached a temperature that will not scald the fingers, the gelatin will be dissolved. It is now removed from the water-bath and cooled until the fingers can be comfortably held in it for some time—about 50° C. or lower. When the gelatin is thoroughly dissolved, the fluid will require re-alkalinization; as gelatin is constantly acid, the previously alkaline bouillon is rendered acid. The alkalinization must be most carefully done, otherwise the gelatin may fail to solidify when finished. Again, one must be sure that all gelatin is dissolved before alkalinization or, later, the reaction may be found acid. It must be but *faintly* alkaline. If by accident the fluid be made

too alkaline, a few drops of dilute acetic acid will correct the error. When the reaction is found satisfactory, the white and finely-broken shell of one egg is thoroughly mixed in with the gelatin; this is heated to the boiling-point in a water-bath, followed by boiling over the naked flame (which is best distributed by a wire gauze) for at least one half of an hour; the water lost by evaporation is made up, and enough of the mixture filtered to half fill a good-sized test-tube; this is boiled repeatedly for several minutes, to see that all the albumin is coagulated, the reaction as desired, and that the gelatin remains clear; if so, the remainder is filtered and filled into test-tubes. When properly made, gelatin is the clearest solid medium at present attainable. It is liquid at temperatures above 22° C., and can not, for this reason, be incubated. As some bacteria liquefy gelatin and others do not, it constitutes a test culture medium of the greatest value.

Beef-peptone-agar.—Agar-agar is a gelatinoid substance derived from a Japanese seaweed. It is used for making culture media solid in the following manner: To 1000 c.c. of bouillon add ten gm. of the agar threads cut into fragments not over two cm. in length; place at once to boil over the naked flame, stirring frequently to prevent burning and the threads adhering to the bottom of the pan. It usually requires about an hour to secure perfect solution, without which filtration is impossible. Longer boiling does no harm, the quantity of the medium being maintained by adding, from time to time, enough water to compensate for that lost by evaporation. When fully dissolved it is filtered. As it filters with much more difficulty than gelatin, and as the same precautions are necessary, I have deferred the description until now. A good, heavy, preferably already-folded filter (machine-folded filters are by far the best) is carefully opened and adjusted in the funnel, then, with the greatest care, thoroughly moistened with boiling water; a moment is allowed for the contraction

of the filter, which always takes place; it is then again moistened with boiling water, the excess poured off, and the agar or gelatin poured down a glass rod onto the *side* of the filter,—*not* into the center and never rapidly, as either will probably break the filter. In the case of agar it is best to have it boiling and add but 250 c.c. or less to the filter at one time, keeping the remainder hot in the water-bath and heating to boiling just before pouring into the filter. Gelatin can not be boiled very long or it may fail to gelatinize; with agar this danger is not present. Gelatin burns to the pan unless carefully watched; agar may do so, but less frequently. Gelatin should always be cleared by an egg; agar may be, but it is not necessary. Agar solidifies at about 42° C., and melts only at near the boiling-point; it is not so clear as gelatin, but, as it can be incubated, has many advantages. It remains solid when prepared with glycerin bouillon, which gelatin does not always do.

FIG. 146.—TEST-TUBE BASKET MADE OF TINNED METAL, FOR HOLDING TEST-TUBES.

These baskets should be 125 by 100 mm., and 150 mm. high.

Culture Containers.—Cultures may be made in bottles, flasks, or test-tubes; the last two are the most used. If perfectly new, a thorough rinsing in clean water will suffice; if the tubes have contained cultures, or have in them cultures either growing or dead, they should be placed in the sterilizer for a couple of hours, with the cotton plugs in place; remove from sterilizer, take out the plugs, pour out the contents of the tubes, and boil one hour in a two per cent. solution of washing soda; wash with test-tube brush and rinse in several changes of clean water; rinse in a one per cent. solution of hydrochloric acid; carry through several changes of water, and set up to dry with bottom upward. When dry, plug

with cotton; for this purpose we use ordinary cotton batting, clean and free from the cotton hulls. Absorbent cotton need not be used. A more or less square or octagonal disc of cotton, about ten cm. in diameter, has its corners folded into the center so as to make a plug twice as long as the diameter

FIG. 147.—DOUBLE WALL HOT-AIR STERILIZER, FOR STERILIZING TEST-TUBES, GLASSWARE, AND OTHER LABORATORY APPLIANCES AND INSTRUMENTS.

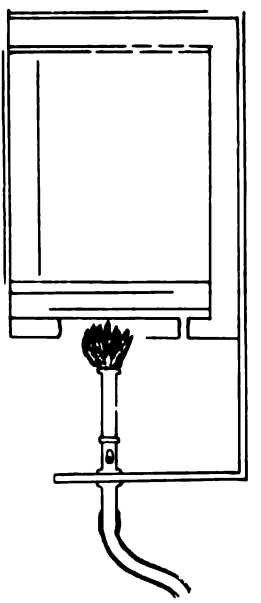


FIG. 148.—DIAGRAM OF INTERIOR OF HOT-AIR STERILIZER.—(*Coplin and Bevan.*)

The construction must be such that a jacket of hot air surrounds the inside chamber, and thereby assures an equal distribution of heat to the interior.

of the tube or the neck of the flask. The plug should fit so tightly that the tube or flask can be lifted safely by the cotton plug, which should enter the mouth to a distance equal to twice the diameter of the tube or the neck of the bottle or flask, and should project at least one cm.

The test-tubes used for cultures should be of the best

Bohemian glass, with a lumen of 13 mm. to 15 mm., and 130 mm. to 150 mm. in length. The flasks should be of the Erlenmeyer form, with a capacity of 100 c.c. Larger sizes, 250 c.c. to 1000 c.c., will be needed for storing media.

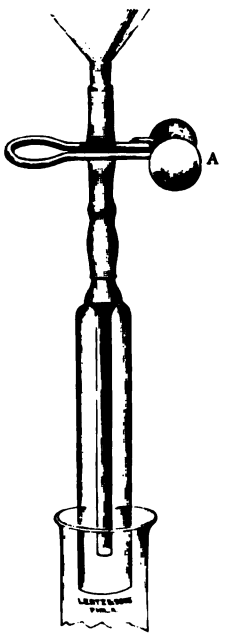


FIG. 149.

Apparatus to be attached to the lower end of a funnel, as shown in the cut, for use in filling test-tubes. The outside glass tube prevents the medium flowing from the inside tube, coming in contact with the mouth of the test-tube during introduction or withdrawal. A. Mohr's spring pinch-cock.

After clearing and plugging, the tubes and flasks are put in the hot-air sterilizer for twenty minutes at 130° C. In the absence of a hot-air sterilizer any cooking oven may be used, leaving the tubes in the oven until the cotton just begins to brown, a temperature which approximates 140° C. The tubes are now ready to receive the medium. An ordinary percolator or funnel has a rubber tube, ten cm. long, connected to the tubulature at the bottom by means of a perforated cork and a short glass tube; at the lower end of the rubber tube a second glass tube is connected so that it projects about ten cm. below the rubber tube; the latter is then collapsed by means of a thumb pinch-cock (Mohr's spring pinch-cock). The liquefied medium is poured into the percolator; the test-tubes are then arranged in the baskets at the side of the percolator. A test-tube or flask is grasped by the left hand, preferably the thumb and index finger; the cotton is rotated and loosened by means of the thumb and index finger of the right hand, and removed by grasping the projecting tip between the ring and little fingers of the right hand; the tube is now carefully slipped over the filling tube from the percolator, *care*

being taken that no fluid comes in contact with that portion of the tube into which the cotton plug is to go; relax the pinch-cock and admit to the test-tube or flask the desired quantity, close the pinch-cock, remove the tube, *using the same care to avoid wetting the mouth of the tube,* and re-insert the cotton plug. This is repeated until the desired number of tubes or flasks are filled. If any of the medium is left over it may be run into a flask, sterilized as will be directed later, and preserved for future use. The amount of medium placed in each tube varies with the medium and the purpose for which it is intended. For some purposes a measured quantity will be needed, but for ordinary purposes the tube should be filled about half full of bouillon or gelatin, with agar to a depth equal to a little more than twice the diameter of the tube. Flasks should never be more than half full when intended for culture, and often very much less will be abundant.

Sterilization.—The Arnold steam sterilizer or the autoclave is used. If the former is used, fractional sterilization is best, keeping filled tubes in the steam chamber, at 100° C., thirty minutes a day for three successive days; in the intervals between sterilizations they are kept at room temperature. The object of this is to destroy all organisms in the adult or fully-developed stage. It is known that spores are not destroyed by a temperature of 100° C. unless it be very long applied; any spores which escape the heat on the first day have time to develop by the second day, or, to assure their being caught, a third sterilization is resorted to. Experience teaches that this is usually sufficient; however, the tubes should be watched for three or four days, and, if any of them show growth, the process should be repeated for all.

By means of the autoclave a temperature of 130° C. is obtained in the steam chamber, which, in from twenty to thirty minutes, destroys both fully-developed bacteria and their spores; it is of great convenience for bouillon, agar, potatoes,

milk, and many other culture media, but can not be used for blood-serum or gelatin. The latter usually fails to gelatinize after being subjected to the high temperature; indeed, gelatin must always be sterilized with the greatest care, as prolonged exposure, even to the temperature of 100° C., should be avoided. Potatoes require prolonged exposure to high tem-

FIG. 150.—ARNOLD'S STEAM STERILIZER FOR STERILIZING CULTURE MEDIA, ETC.

perature, as they usually contain earth organisms difficult to destroy.

In order to increase the surface area of media containing agar or blood-serum, the tubes, while the medium is in a liquid state, are inclined with the mouth just high enough to not permit the agar flowing up to the cotton; when "set" they may be stood on end, as other tubes.

Dunham's Peptoné Solution.—Rub up in a mortar five

gm. of salt and ten gm. of peptone, with enough water to make a paste; finally, dilute to 1000 c.c., boil, and filter. As a rule, the filtrate is neutral or alkaline; in either case, after sterilizing as already described for bouillon, it is ready for use.

For plating it is always best to have on hand a number of tubes of gelatin and agar, each tube two-thirds full.

Pure Cultures.—A pure culture is one containing but one

FIG. 151.—ARNOLD'S STEAM STERILIZER, BOSTON BOARD OF HEALTH FORM. This is the most convenient and the best sterilizer for general laboratory purposes.

variety or form; for example, a pure culture of the tubercle bacillus must contain no other germ. Where two kinds of bacteria are growing together, the culture is said to be a *mixed culture*. Under nearly all conditions various organisms are found together, and, in order to separate them, we must resort to plating. The object to be attained is the separation of each germ, in order to enable it to grow into a colony by

itself; so that, if the original mixture contained three kinds of bacteria, we may obtain three kinds of colonies, and from these obtain cultures which have but the one variety—that is, a pure culture of each.

Bottle Plates.—Any good, clear, flat-sided bottle will do.

FIG. 152.—AUTOCLAVE OR DIGESTOR USED FOR STERILIZING BY STEAM UNDER PRESSURE. The lid is held in place by three winged nuts, which are thrown down to the side in order to raise the lid. The solid copper chamber on the inside has placed in it two liters of water, and the material to be sterilized is placed upon the tray with perforated bottom shown at the side of the cut; this is then placed inside of the autoclave and the lid closed down and secured by the winged nuts; the gas is now lighted and the heat applied until steam escapes from the small cock at the left, which is then closed. The pressure within the apparatus now rises until the safety-valve, which may be set at any pressure, blows off. Sterilization by this means may be secured, at temperatures ranging from 100° C. to 140° C., in from twenty to forty minutes.

The capacity should be about 500 c.c.; clean, plug with cotton, and sterilize in hot-air sterilizer; charge with gelatin or agar, usually about 20 c.c. Sterilize as already directed for culture media, and set the bottle aside until wanted for plating; to prevent drying of the medium, the cotton may be pushed

downward in the neck so as to admit a short rubber stopper. As a rule, the bottle will be used within one month, during which time it will not dry injuriously. When ready for use, three bottles will be needed. Liquefy the medium in the sterilizer or water-bath; cool to 50° C. or below, inoculate the first bottle with a small loop of the mixed culture or suspected material, as pus or blood, stopper the bottle with the cotton plug, and shake to thoroughly mix; inoculate the second bottle by carrying a loopful from the first to the second, replace the plug, and shake; and in the same manner inoculate a third bottle from the second, and shake as before. Lay the three bottles on the flat side; the medium will spread out and cover the side of the bottle; label the three bottles *a*, *b*, and *c*, the first being *a*.

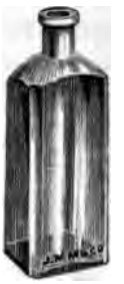


FIG. 153.—BLAKE BOTTLE USED FOR BOTTLE-PLATES.—(*Coplin and Bevan.*)

Petri Dish Plates.—Three or more test-tubes containing sterile agar-agar or gelatin, filled to within an inch or so of the cotton, as already directed, are placed in a water-bath or sterilizer and the contained medium liquefied; while this is in progress an equal number of Petri dishes are sterilized in the hot-air chamber and allowed to cool. The liquefied medium is cooled to under 50° C. A tube is inoculated with the material to be plated, as directed for bottles; from the first tube a second is inoculated, and from the second a third, and so on, each tube having the medium thoroughly mixed by using the inoculating needle as a stirrer. Remove the cotton from the first tube and pass the lip of the tube through the flame; raise the lid of a sterile Petri dish just

FIG. 154.—DISH DEVISED BY PETRI.

Used almost exclusively for plating; the most convenient diameter is 120 mm.

enough to get the mouth of the tube under it, and quickly pour the contents of the tube into the dish, which is then gently tilted from side to side, allowing the medium to flow over the bottom and cover it fully. A second dish receives in the same way the contents of the second tube, and so on, through as many tubes as may be desired. The plates are labeled as directed for the bottles.

Esmarch's Tube Plates.—Three or more tubes of sterile agar or gelatin, each tube not containing over two or three c.c. of the medium, are liquefied and inoculated as directed for the Petri dish method. A block of ice, with a flat or nearly flat upper surface, has a channel made in it by laying a test-

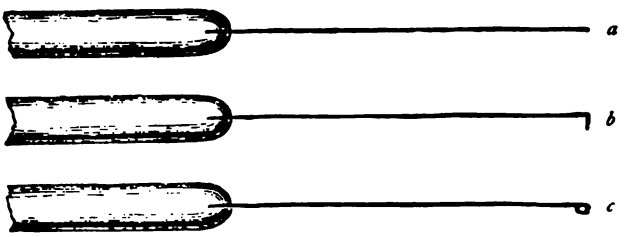


FIG. 155.—PLATINUM INOCULATING NEEDLES MOUNTED IN GLASS RODS.
Showing the shape of the ends as may be found useful for: *a*, stab cultures and stroke cultures; *b* and *c*, stroke cultures and smear cultures.

tube of the same size as those to be used, filled with hot water and corked, upon the top of the ice, the corked end projecting beyond the edge of the ice; this tube is rolled over and over in the same spot until a channel is so made as to half bury the tube, the bottom end being a little lower than the cork end. Into this channel one of the infected tubes is laid so that the medium flows up to within two cm. of the cotton but *does not touch it;* the tube is then rolled, at first slowly, then more quickly, until, within the first minute, it is spun rapidly; the medium is in this way congealed over the entire inside of the tube nearly up to the cotton; if the latter comes in contact

with the medium it prevents easy removal of the plug by making it stick to the side of the tube. Each tube is treated in the same way, after which it is labeled as directed for other plates. When set, the tubes are placed on end. With gelatin this can be quickly done; with agar-agar, however, the tube must be kept in a nearly horizontal position for several hours, generally over night, otherwise the agar-agar may slip down.

After the plates are made by either of the above methods we have to await the growth of the colonies; agar may be incubated. At the end of a varying period the colonies appear, as distinct dots, in and on the culture medium. In plate *a* they will commonly be too close together to be distinct; plates *b* and *c* will be better. Selecting a colony which is alone, transplant this into a test-tube in the following manner:

Take the platinum needle and heat its entire length to redness, at the same time heating all of the attached glass rod which is likely to go into the test-tube, bottle, or dish. If the colony to be removed is within a bottle or test-tube, it will be best to have bent the tip of the inoculating wire like the letter L; immediately after sterilizing the needle, holding it like a pen in the right hand, take the bottle and test-tube or both test-tubes in the left hand; remove the plugs from the tubes or bottles by grasping the projecting cotton of both tubes between the middle and ring fingers and the ring and little fingers of the right hand; pass the lip of the bottle or tube through the flame to burn off any adhering dust; pass the needle into the bottle or tube, and just touch the colony from which it is desired to obtain a culture; this will infect the needle; quickly withdraw the needle and pass it into the tube upon which it is desired to inoculate the growth. The inoculation made may be: (*a*) a **streak** or **stroke culture,** in which case the needle is drawn from below upward in a straight line over the slanting surface of an agar-agar or blood-serum tube; (*b*) a **smear culture,** made by gently rubbing the infected wire over the surface of the med-

FIG. 156.—METHOD OF HOLDING TUBES, COTTON, AND PLATINUM WIRE WHILE INOCULATING SOLID MEDIA.—(*Koch's method, modified from Woodhead.*)

The tubes *c* and *d* are grasped as shown in the illustration. The cotton from *d* is removed with the thumb and index finger of the right hand, and held between the ring and little fingers of the left hand, at *b*; that portion of the cotton which was within the tube is not touched by the fingers but is directed upward. In the same way the cotton is now removed from the tube *c* and grasped by the ring and middle fingers, as at *a*, the same precautions being used as described for the other tube. The lips of the tube are now passed quickly through the flame of a Bunsen burner, to remove any adhering dust, and the platinum wire and the glass rod sterilized in the flame, the rod being heated to a greater distance than it is expected to enter the tube. Supposing that *d* is the tube from which it is desired to remove the culture, and *c* is to receive it: the needle, while still warm, is thrust into the culture medium to one side of the growth to cool the needle; the growth is then touched by the needle, thus infecting the needle, which is quickly withdrawn and the tube *c* inoculated; *immediately upon the withdrawal of the inoculating needle* the cotton stoppers are placed in their respective tubes and the *needle at once sterilized* and set aside. *Never lay down an infected needle.* The tube inoculated is labeled, dated, etc., and set aside for observation. All of this can be done quickly, and the beginner should practise the manipulation on tubes of media which are not infected; if they become infected during the process, his technic is faulty, and should be perfected before working with pure cultures.

ium ; or (*c*) a **stab culture,** made by a straight needle-thrust, from above downward, through the medium. Stroke and smear cultures are the most common on all solid media except gelatin, into which stab cultures are most used. In trans-

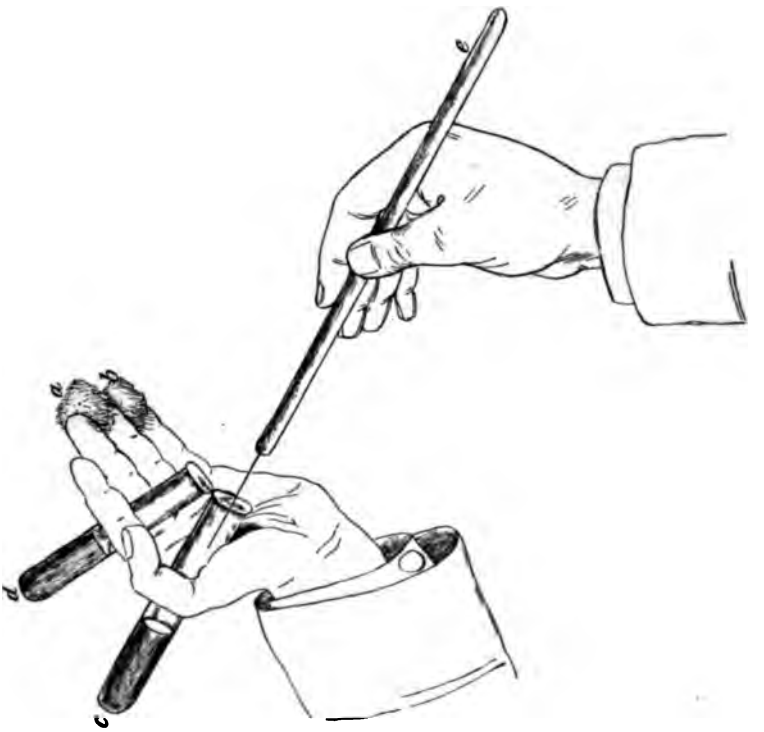


FIG. 157.—METHOD OF HOLDING TUBES, COTTON, AND PLATINUM WIRE WHILE INOCULATING LIQUID MEDIA.

The steps and the lettering are the same as in previous figure. The right hand should not be over the tubes, as it appears in this illustration, but the tubes in the left hand should be so inclined that there will be but little danger of anything dropping into the sterile tubes.

planting from a Petri dish culture, the lid is barely raised enough to introduce the previously sterilized needle, which is then touched upon the colony, removed, and applied to the culture tube as above directed.

The platinum needle used in bacteriologic work consists of a platinum wire, one mm. to two mm. in thickness and five cm. to eight cm. in length, fused into the end of a glass rod about five mm. in thickness and 14 cm. to 18 cm. long. The rod is used as a holder or handle for the loop. The latter is variously curved, looped, or may be used straight, as for stab cultures.

Bacteriologic Examination of Water and Other Fluids.* —Sterilize in the hot-air sterilizer a container, and collect the water for examination. As bacteria multiply very rapidly, the examination should be made as soon as possible after collection; after a few hours' standing, particularly if the weather be warm, the results obtained will be without value as to quantity.

Prepare a dozen Petri dishes and a corresponding number of tubes for plating. Sterilize two burets so graduated as to accurately measure 0.02 to 1.0 cm.

Thoroughly agitate the water to diffuse the bacteria equally throughout the specimen, and fill a buret with the sample under examination. The test-tubes of media, gelatin, or agar-agar having been fully liquefied, are cooled to 45° C. in a water-bath; to each of two of the tubes is added 0.02 c.c. of the infected water; to another pair of tubes 0.05 c.c. of water is added; to another 0.075 c.c.; to another 0.1 c.c.; to another 0.5 c.c.; and to another 1.0 c.c. The tubes are thoroughly shaken, immediately poured in the usual way, and set aside for the colonies to develop. If agar-agar has been used, the plates may be incubated. As soon as the colonies develop they are counted. A Petri dish counting apparatus may be used, or a slate upon which has been ruled a figure like that

* Bacteriologic examinations of water and air are introduced here as being good examples of the practical application of improved plating methods, and that the student may familiarize himself with the technic of preparing plates and securing pure growths therefrom.

shown in figure 158. All the colonies in the plate may be counted or the number determined in one, two, or more of the

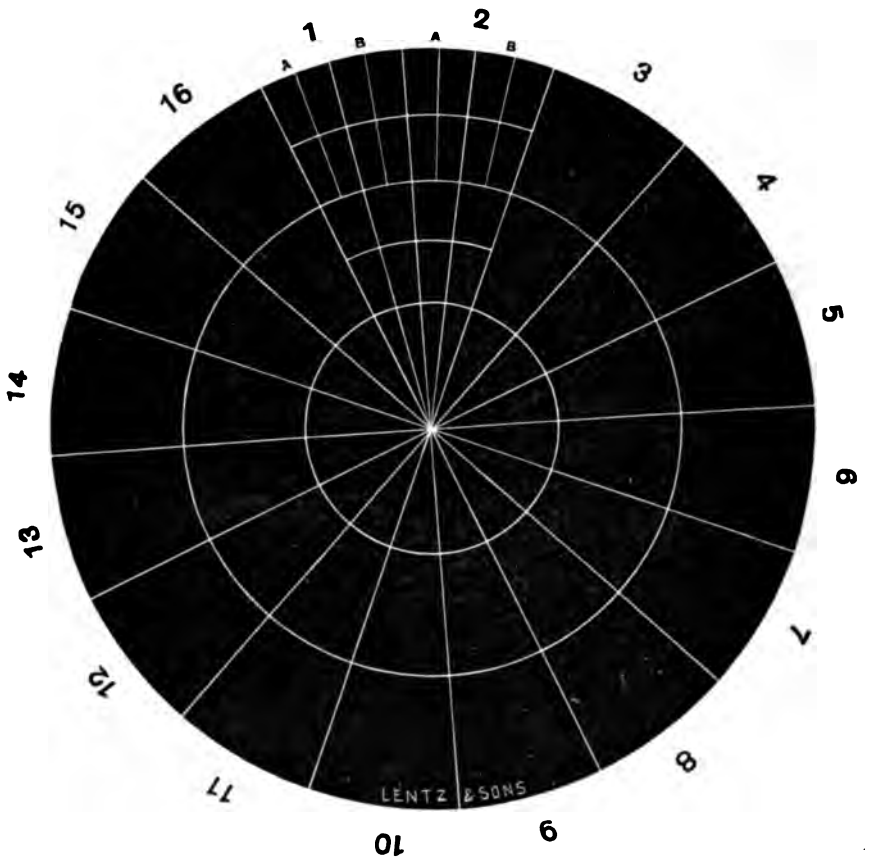


FIG. 158.—APPARATUS FOR COUNTING COLONIES.

Petri dishes are placed upon the ruled circle and the colonies counted as directed in the text. An ordinary slate may be ruled in the above figure and used for the same purpose.

wedge-shaped areas bounded by the radii and the arc, and the resulting number found for one wedge-shaped area multiplied by the total number of divisions—sixteen. The number of

colonies found in the whole plate represents the number of bacteria in the water used for the plate. For example: Several areas counted give an average of 20 colonies to each area; there are 16 areas: 20 × 16 = 320, the total number of colonies in the plate; assuming that the quantity of water used in making the plate was 0.1 c.c., then 1 c.c. will contain ten times 320, or 3200 bacteria. If different quantities of water are used, the result, reduced to the unit, say one c.c., should be approximately the same, one series being a control for another. The above test determines the number of bacteria in the sample.

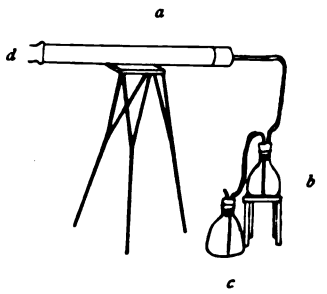


FIG. 159.—HESSE'S AËROSCOPE.

This consists of a hollow cylinder of glass, *a*, 60 cm. in length, four cm. in diameter, plugged with cotton at both ends, sterilized, and charged with a layer of culture, much as the Esmarch plates. The two ends are covered by caoutchouc, one of the rubber caps having a hole to admit a glass tube by which the tube *a* is connected with the gravity flask *b* which is further connected to the flask *c*. The flask *b* is filled with water. When ready for use the rubber cap and cotton plug at *d* are removed, the flask *b* tilted so that the contained water flows into flask *c*, thereby aspirating into the tube *a* as much air as water is allowed to flow from the upper to the lower flask. The tube *a* is now plugged and set aside for colonies to develop. These can be counted and transplanted as in other plate methods. Petri has improved the above by substituting for the tube *a* a short tube packed with sand and sterilized, aspirating air through it, and then mixing the sand with gelatin and pouring into plates. Sedgwick and Tucker use sterilized granulated sugar instead of the sand. The sugar and sand methods give the best results.

If it is desired to find what germs are present in the water, to make the test complete, the colonies are transplanted and studied as already directed when considering pure cultures. (See table illustrating the method of recording principal characteristics of an organism.)

Bacteriologic Examination of Air.—The principle upon which the examination is conducted is to depend either upon sedimentation upon a sterile surface, as a Petri dish containing media,—a very unsatisfactory method,—or to secure the

bacteria in a sterile filter by aspirating through it a known quantity of air. The accompanying figure, with the attached legend, will explain the methods used.

Staining of Bacteria.—The staining of bacteria greatly facilitates the study of their morphologic characteristics. For this purpose we use, almost exclusively, the anilin dyes. Weigert was the first to employ these dyes, and other observers, seeing the distinct advantages which they possessed over other dyes, quickly adopted them.

Those commonly used in the laboratory are fuchsin, gentian-violet, methyl-blue, and a few others; the application of all is practically identical. For stock, it is best to keep the dye as a saturated alcoholic solution. For staining, however, alcoholic solutions are of little value, as they do not seem to have the penetration of watery solutions. The usual strength of solution is two per cent. of the dye dissolved in water; as the dyes are disagreeable to handle, the solutions are commonly prepared by taking a test-tube, 13 to 15 mm. in diameter, filling it about two-thirds full of distilled water, and adding the saturated alcoholic solution of the dye, drop by drop, until the water is so colored that, by ordinary diffuse light, one can barely see through it. This is then poured into a bottle adapted with a Barnes' dropper. (See cut of appropriate stain bottle, p. 56.) The solution so prepared is about 1.7 per cent., and may be used whenever a one or two per cent. solution of the dye is ordered.

One of the most useful stains is the *Koch-Ehrlich anilin-water solution*. This should be freshly prepared each time it is wanted, as it will not keep. Take in a test-tube about 20 c.c. of distilled water; add anilin-oil, drop by drop, shaking thoroughly until no more of the anilin is dissolved, the drops floating on and in the water; filter until clear; usually one filtration will be enough, but occasionally it will require two or three.

Formula for stain:

Saturated solution of anilin-oil in distilled water, 100 parts.
Saturated alcoholic solution of gentian-violet, methyl-violet, or fuchsin, ... 11 "
Alcohol, ... 10 "

As it is not desired to stain laboratory utensils any more than can be avoided, it has been found that practically the same results as those secured by measuring can be obtained by dropping the solutions; 100 drops of the anilin-water, 21 drops of the alcoholic solution of the dye, and 20 drops of alcohol.

Löffler's Alkaline Methyl-blue Solution:

Saturated alcoholic solution of methyl-blue, . . 3 parts.
One to 10,000 aqueous solution of caustic potash, 100 "

Ziehl's Carbol-fuchsin.—Rub up 1 gm. of powdered fuchsin with 10 c.c. of alcohol in a glass mortar; dissolve 5 gm. of crystalline carbolic acid in 100 c.c. of distilled water; mix the two solutions and the stain is ready for use.

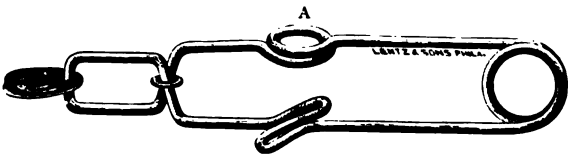


FIG. 160.—LATEST IMPROVED FORM OF STEWART'S COVER-GLASS FORCEPS.
Method of holding cover-glass and applying the stain. If the cover-glass be grasped with the film or spread side toward the side of the forcep which has the circular bend intended to fit the thumb and shown at A, there will be no danger of losing trace of the side which contains the spread, as this side of the forcep is practically always upward.

To Stain Bacteria.—Thoroughly cleanse a cover, dry and polish it; grasp it with Stewart's cover-glass forceps and pass it through the flame a number of times to burn off any bacteria or other organic material which may be on it; avoid heating too much, as the cover may warp or crack. Spread on this, with a previously well-sterilized platinum loop or

needle, a thin film of the material; permit it to dry *without using any artificial heat.* It is then "fixed" by passing through the flame, as follows: Stand about 30 cm. from the flame and carry the cover-glass through a circle, the diameter of which is represented by the distance between the flame and the worker; pass it through the flame three times. Stain two to ten minutes; wash thoroughly in water, dry, and mount with the film side downward.

Weigert's Method for Sections of Tissue Containing Bacteria.—Place sections from six to eighteen hours in a one per cent. aqueous solution of any of the basic anilin dyes; after removal from the stain, wash in one-half saturated solution of potassium carbonate, then in distilled water, next in 60 per cent. alcohol, and finally dehydrate in absolute alcohol. Clear in oil of cloves or creosote, and mount. Heating the stain or using a stronger solution will hasten the staining process, though it may not be so satisfactory.

Gram's method may be used for either cover-glass films or sections. Stain in the Koch-Ehrlich solution (formula given on preceding page) from two to five minutes, in most cases, to twelve or twenty-four hours in others; rinse for a moment in water, and apply Gram's solution.

Gram's Iodin-iodo-potassic Solution:

Iodin,	1 part
Potassium iodid,	2 parts.
Distilled water,	300 "

As soon as the section becomes a dark brown, wash in 60 per cent. alcohol, dehydrate in absolute alcohol, clear, and mount. After washing in 60 per cent. alcohol, sections may be contrast stained with carmin or hematoxylin, or with a one per cent. aqueous solution of vesuvin, or Bismarck brown.

Neisser's method of spore staining consists in preparing the cover-glass as before, floating it upon the Koch-Ehrlich solu-

tion in a watch-glass, and heating to near the boiling-point for an hour. It is next washed in water and decolorized by a solution composed of 25 parts of hydrochloric acid and 75 parts alcohol. This removes the stain from the bacilli but leaves the spores stained, if not allowed to act too long. The preparation is next stained with methylene-blue, washed in water, dried, and mounted.

Flagella Staining.—Löffler's method requires two fluids, the first being a mordant, the second the stain. First solution consists of:

Aqueous solution of tannin (20 gm. tannin to 80 c.c. water),	10 c.c.
Aqueous solution of ferrous sulphate, saturated in the cold,	5 "
Saturated alcoholic solution of fuchsin,	1 "

The coloring solution is composed of saturated solution of fuchsin in anilin-water, to which is added a few drops of caustic soda (1 : 1000) until opalescence commences. The mordant is applied to the cover-glass film, heating slowly over the flame for one minute. It is not necessary for the liquid to boil. Wash in distilled water and then in alcohol. Stain by placing on the film a drop of alkalized staining solution, heating again gently for one minute; wash in distilled water, dry in air, and mount.

Different species of bacteria require an acid or alkaline reaction to the mordant, and for this purpose two solutions are necessary: (1) Caustic soda, one per cent. aqueous; (2) an aqueous dilution of sulphuric acid, of which one c.c. will just neutralize one c.c. of the alkaline solution. For spirillum of cholera, ½ to one drop of the acid solution to 16 c.c. of the mordant; for bacillus typhosus, two c.c. of the alkali to 16 c.c. of the mordant, and so on; the number of drops of either solution can only be determined by experiment upon the organism in question. The bacillus pyocyaneus and many

varieties of the spirillum require an acid reaction, while bacillus typhosus, bacillus subtilis, bacillus of malignant edema, and bacillus of symptomatic anthrax require an alkaline reaction.

Pitfield has recommended the following stain for flagella, using but one solution for mordant and stain :

(A) Saturated aqueous solution of alum, . . . 10 c.c.
Saturated alcoholic solution of gentian-violet, 1 "

(B) Tannic acid, ... 1 gm.
Aqua dest., ... 10 c.c.

These are made separately, filtered, and mixed. This stain is applied and heated gently almost to boiling-point, washed in water, dried, and mounted.

Microscopic Examination of Stained and Unstained Mounts.—In tissues stained by any of the methods given, the location, under a low power,—$\frac{1}{6}$-inch objective,—of bacteria can often be inferred by agminated areas of the stain known to stain such organisms. Having located such areas, a higher power may be used. Always begin the examination with a low power.

(For description of microscope and method of using same, see page 59.) To use the $\frac{1}{12}$-inch oil immersion objective: First, with a lower power, find and accurately center some object in the field upon which to focus ; rack the tube upward until the objective is four or five cm. from the slide ; rotate the nose-piece so that the $\frac{1}{12}$-inch objective drops into the optic axis of the instrument. Place the stand erect so as to make the stage level. Place on the cover-glass a drop of cedar oil, at such a point that when the objective is racked down it will touch the drop of cedar oil at its center. The objective is now racked down into the cedar oil ; looking into the instrument, adjust the light so that the field is well illuminated, the light uniformly distributed, but not too brilliant or

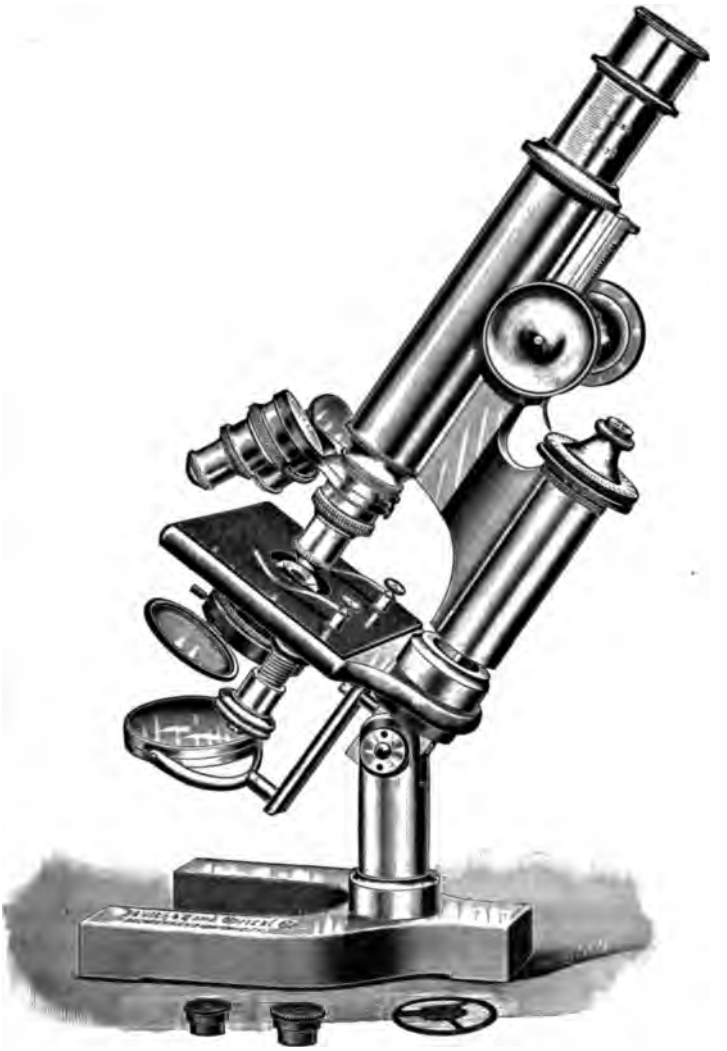


FIG. 161.—MICROSCOPE SUITABLE FOR GENERAL PATHOLOGIC AND BACTERIOLOGIC WORK.

As shown here, it is fitted with three objectives, a ⅔ of an inch, ⅙ of an inch, and $\frac{1}{12}$ of an inch mounted on a triple nose-piece. For bacteriologic work the $\frac{1}{12}$ of an inch oil-immersion objective is necessary, but for normal and pathologic histology only the ⅔ of an inch and ⅙ of an inch will be needed. The stand here figured is also fitted with an Abbe condensor, iris diaphragm, and blue-glass. (For method of using low powers and for description of parts, see page 59. For method of using $\frac{1}{12}$ of an inch oil-immersion objective, see text.)

glaring; this, if present, should be overcome by closing the iris diaphragm until a soft, even illumination is obtained. Now, with the fine adjustment, slowly focus upward but one or two turns of the milled head; the object should come into view. If it is indistinct or hazy, try re-adjusting the iris diaphragm or the light, or the Abbe condenser may be moved downward or upward until the desired effect is secured. In examining the stained specimens of bacteria the iris diaphragm is kept open; for unstained specimens it is choked down to but little light. The successful study of any specimen is largely dependent upon securing perfect adjustment of all the parts of the microscope, and particularly the illumination. In case the field fails to clear up after careful adjustment of the instrument, examine the lenses to see that they are not dirty.

Gas Formation.—The development of gas may well be investigated in connection with our study of yeasts. Thus, if a saccharometer charged with a sterile culture fluid containing glucose be inoculated with the saccharomyces cerevisiæ, gas will collect in the measuring-tube, showing its production by the growth of the yeast. In addition to the production of gas it can be shown that the fluid contains other substances; simultaneously with the gas production alcohol is elaborated. The equation is written as follows:

Glucose	=	Alcohol	+	Carbon Dioxid.
$C_6H_{12}O_6$		$2C_2H_6O$	+	$2CO_2$

The study of gas formation is conducted for other organisms after the same method as described for the yeasts; while saccharine fluids are mostly used for this study, other media have also been found available.

Gelatin or agar-agar *shake cultures* are sometimes used to detect gas formation. Either medium is liquefied, cooled to below 50° C., and inoculated while liquid; it is then thoroughly agitated and allowed to solidify. The growth of those

organisms producing gas will be evident by the appearance of small gas bubbles throughout the medium. The test is, at times, facilitated by using a medium containing glucose, in which case the reaction may be identical with that previously described; in many cases it is, however, a much more complex problem.

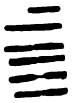


FIG. 162.—PROPAGATION BY FISSION.—(*Coplin and Bevan.*)

Reproduction of the schizomycetes is principally by the process of *fission; i. e.*, a cell having reached its full development simply divides into two or more segments. We also have reproduction taking place by *spore formation.* There are two kinds of spores described at the present time: (1) Arthrospores, and (2) endospores.

Arthrospore formation is described by de Barry and Hueppe as occurring in cocci. In certain chain cocci there are a few cell elements which acquire those characteristics common to spores without any apparent differentiation of cell protoplasm. They appear larger than the other elements of the chain; their borders are more sharply defined, and the cell wall appears to be thicker; they possess a much greater resistance than the other cells, to all conditions incompatible with life, and their protoplasm is darker or more highly refractile. When these bodies are removed from conditions which brought about the death of the other chain elements, and they are placed in favorable soil, they will develop the characteristic chains.

If the nutrient media upon which the bacterium Zopfii is being cultivated becomes exhausted, the organisms are, by a process of fission, resolved into a number of more or less spheric bodies possessing the properties of spores.

Endospore formation is the development in an organism of spheric or oval bodies possessing unusual resistance to conditions incompatible with the life of the mature organism. Usually the spores make their appearance only when germ

plasm manifests degenerative changes and becomes granular. The spore appears at first as a small, bright point, which gradually increases in size until its diameter may exceed that of the parent cell. Frequently the spore develops in the center of the organism, when, if the organism is a bacillus, it may appear spindle-shaped. If the spore develops at one of the poles of a bacillus, the organism will appear club-shaped or pendulum-like, a characteristic of the bacillus tetani. The spores, however, may develop at short intervals through the entire extent of the bacillus, when the organism will present a bead- or chain-like appearance, as seen in anthrax. Spores, under favorable conditions, always develop into organisms identical with those from which they were derived.

FIG. 163.—FROM CULTURE OF BACILLUS MEGATHERIUM, SHOWING DEVELOPMENT OF SPORES WITHIN THE CAPSULE OR BACILLARY ENVELOPE, WHICH, LATER, BREAKS UP AND LIBERATES THE SPORES.—(*Coplin and Bevan.*) × 800 diameters.

Endospore formation occurs principally in bacilli, but also in spirilli. Zopf has described the formation of endospores in certain micrococci, and Escherich in the sarcina pulmonum.

The processes of reproduction, as seen in yeasts and molds, are described and figured with those fungi.

We can not distinguish between the many species of any one kind of organism by morphologic peculiarities alone, therefore we must develop biologic characteristics to serve us as a guide to their recognition. Thus, for instance, we know there exist several varieties of the micrococcus pyogenes, which morphologically are identical, and, were it not for certain biologic peculiarities, we could not tell one from the other. Those points commonly worked out will be found tabulated a few pages further on.

Micro-organisms forming pigment in the process of growth and development are known as **chromogenic bacteria** or **chromogens.**

Zymogenes or **zymogenic bacteria** are those capable of inducing fermentation.

Pathogenic bacteria are the disease-producing bacteria.

The faculty of producing color, fermentation, or disease, are simply properties, and one or all may be possessed by a single organism. Furthermore, an organism, under varying conditions, may be chromogenic or non-chromogenic, zymogenic or non-zymogenic, pathogenic or non-pathogenic. Again, an organism which is pathogenic for one animal may be wholly destitute of this property when injected into an animal of another species.

Aërobic and **anaërobic** are terms introduced by Pasteur to denote that an organism requires the presence or absence of oxygen as an essential to its growth. It was proposed at one time to classify bacteria as aërobic or anaërobic organisms, but it was soon discovered that certain organisms might be cultivated either in the presence or absence of air, though they usually showed a preference for one or the other condition. This led to the introduction of the terms facultative and obligate. An *obligate organism* requires absolutely one or the other condition. A *facultative organism*, while showing a marked preference for one condition, may develop under the other. Although the hope of thus classifying bacteria has been abandoned, the terms are retained, and are now used simply to describe such peculiar properties of certain species.

Anaërobic Cultures.—*Novy's Apparatus.*—Petri plates, Esmarch plates, or culture-tubes are placed inside, the dome is put in position and secured by the vise-like clamps, D, D; the glass stopper is turned, as shown in the cut. The tubulature not having the L-shaped extension downward is connected with the hydrogen generator, and a constant stream of gas is carried through the apparatus for some hours. As soon as the air is displaced, the stopper, C, is turned one-fourth of a turn, thus cutting off the connection between the tubulatures on

the side of the neck and the inside of the apparatus. If

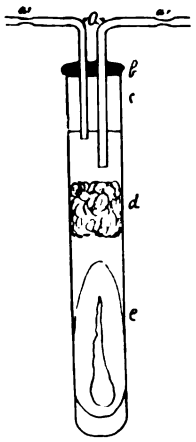


FIG. 164.—STERNBERG'S ANAËROBIC CULTURE TUBE.

The tube is an ordinary culture tube of rather large size. The culture medium, *e*, is inoculated, the cotton-plug *d*, while at the top of the tube, is cut even with the glass and held in the flame until thoroughly browned, to fully sterilize it, and is then pushed down into the tube with a sterile glass rod. A cork, *c*, with two perforations, through which pass the L-shaped tubes *a*, is fitted to the mouth of the test-tube and sealed with wax at *b*. Hydrogen gas is now passed through the apparatus for an hour or so, depending upon the size of the tube, until all of the air is displaced; the entrance and exit tubes are then sealed at *a'*, *a'*, by fusing the glass. The advantage of this simple method is that any tube can be used and any of the common media in use in the laboratory.

FIG. 165.—NOVY'S APPARATUS FOR ANAËROBIC CULTIVATION OF PLATES AND TEST-TUBES.

This apparatus consists of the following parts: *A*, the base, a solid glass cylinder having a capacity of about one liter and ground at its upper edge with a flange to make an air-tight joint with, *B*, the dome, the two being clamped together by the vise-like clamps *D*, *D*, the joint being more perfectly assured by rubber bands. The top of the dome *B* arches into a neck like that of a bottle and is closed by *C*, which is an ordinary ground-glass stopper ground into the mouth of the neck, to the dome *B*. Through the side of the glass stopper *C*, two openings, so arranged than when *C* is turned, as shown in the cut, the openings permit gas to pass into the interior of the apparatus through either of the tubulatures shown at the side of the neck. On the inside of the stopper an L-shaped tube is fused so that any gas carried into the apparatus through that tubulature passes below the level of the opposite tubulature.

carbon dioxid is used instead of hydrogen, it is admitted through the tubulature which communicates with the inside

through the L-shaped piece. I have fancied that the exclusion of air when using hydrogen was facilitated by attaching to the L-shaped piece a soft rubber tube extending to the bottom of the apparatus; as air is much heavier than hydrogen, this device causes the gas admitted through the opposite tubulature to displace the air more rapidly.

Motility.—Many bacteria possess the power of locomotion. The cocci, bacilli, and rigid spirals are propelled by the exceedingly rapid vibratory motion of thin, lash-like processes, extending from the sides or poles of the organism, called flagella. Certain of the flexible spirilli possess the power of moving from place to place by (1) a rotary motion in their long axis, or (2) by an undulatory or snake-like movement.

Hanging Drop Cultures.—If a drop of liquid culture be placed on a slide and covered in the usual manner, an

FIG. 166.—DROP CULTURE SLIDE.
75 × 25 mm., of polished plate glass, with cavity 18 mm. in diameter.

examination with a high power will usually demonstrate the motility of an organism. This crude method is not accurate, as heat currents always occur in fluids under a cover-glass, and may mislead the observer. For demonstrating motility the drop culture-slide is used. This consists of a thick slide of the same dimensions as the ordinary microscope slide, with a hollow ground in its center. A clean cover-glass is grasped in the forceps, and passed through the gas flame to sterilize it. The concave slide is prepared in the same way, allowed to cool, and around the concavity is painted a thin line of any non-volatile oil—ordinary sperm oil, vaselin, or, where the slide is to be incubated, paraffin or oleum theobroma liquefied by gentle heat. A droplet of the culture in bouillon or Dunham's solution is placed in the center of the

cover-glass, which is then inverted over the hollow slide, care being taken that the droplet is very small,—not larger than a small pin's head, so that it will not sway from side to side,—and that it does not come in contact with the slide at any point. With the stage of the microscope perfectly horizontal, the droplet is carefully focused upon. The moving bacteria can be easily seen, provided the illumination is satisfactory; the iris diaphragm should be closed to admit but little light, otherwise the field will be so flooded with light that the small, colorless bodies—the bacteria—may escape detection. It is often advisable to center the drop with a low power, say a ½- or ⅔-inch objective, before attempting to focus with a high power. If the organism is growing on a solid medium, a small part of the culture is mixed with the bouillon or Dunham's solution on a sterile cover, and the hanging drop prepared from the mixture.

The "hanging-drop culture"—as such the above is known—may be incubated and kept under observation for a long time if care is used to avoid infection during its preparation and to exclude bacteria by a perfect oil seal. By observation in the incubator, bacteria can be seen dividing, yeasts watched while forming and throwing off buds, and other observations made (see Widal's test, p. 91).

Liquefaction.—Those bacteria which in their growth liquefy Koch's flesh-peptone-gelatin are known as liquefying. They probably elaborate a ferment which has this property. Organisms not having this property are known as the non-liquefying bacteria.

The power of **producing gas** is marked in some forms of bacteria, and absent in others (see page 271).

Some bacteria **coagulate milk,** and this may be used as a test in studying species.

Reaction.—During the growth of many organisms the

reaction of the culture medium is changed. This test is applied by adding an indicator to the fluid, or other medium, and observing if the color of the indicator changes. The two indicators most commonly used are litmus and phenolphthalein ; the former is kept in stock as a tincture, and the latter as a 0.1 per cent. solution of the salt in 50 per cent. alcohol. To apply the test a number of tubes of culture media, milk, bouillon, or, what is best of all, Dunham's solution, are prepared ; although much less suitable, solid culture media, as gelatin, agar-agar, or potato may be used. In bulk, some of the medium, enough to fill several test-tubes of the size intended for use, has added to it enough of the indicator to faintly, but clearly, show the reaction ; one lot of the medium should be but faintly acid, very dilute acetic acid being used to acidify ; another lot should be rendered faintly alkaline by the use of one per cent. caustic potash, while a third lot is neutral. With great care sterile media may be sensitized without subsequent sterilization ; as a rule, however, after sensitizing it will be necessary to resterilize the test medium. The same quantity should be in each tube. A number of tubes belonging to each series are inoculated with the germ in question, and several are left as test or control reserves. In the course of a few days, often in less than twenty-four hours, it will be observed that the reaction of the two series is changing. If the germ produces an alkaline reaction, the neutral series evinces the change first, followed by the acid series becoming less markedly acid and, in some instances, eventually manifesting a clearly-defined alkaline reaction. The alkaline series may show a slight intensification of the alkaline reaction or may not change at all. The control tubes should remain constant. If the organism produces an acid, the reaction given above will be reversed.

Rosolic acid is also used as an indicator ; the stock solution

is prepared by adding 0.5 gm. of the acid to 100 c.c. of 80 per cent. alcohol. Its use is the same as the above; it pales when acid, intensifies its rose color when alkaline.

Indol.—Among the chemic tests applied for the identification of bacteria is that for indol. Several tubes are charged with seven c.c. of Dunham's solution sterilized, and three or four inoculated with the germ under investigation, and twice the number reserved for controls. After twenty-four hours, add to one of the controls ten drops of chemically pure sulphuric acid, and to another one c.c. of a sodium nitrite solution freshly prepared, and made by dissolving one gm. of chemically pure sodium nitrite in 10,000 c.c. of ammonia-free water. To the second tube also add ten drops of sulphuric acid. Both tubes should be watched for fifteen or twenty minutes; no color should develop, as they contained no indol. To one of the inoculated tubes add the sulphuric acid, and if, in from ten to twenty minutes, no reaction occurs, add the sodium nitrite solution as previously directed; if indol be present, a distinct rose color appears. Occasionally the rose color may appear without the addition of the sodium nitrite, in which case the organism has not only produced indol, but also a reducing agent, commonly a salt of nitrous acid.

Thermal Death-point.—Each organism has what is known as its optimum temperature, at which the growth is most luxuriant and above or below which it becomes less and less free as the change progresses. Eventually temperatures are reached so high or so low that growth is arrested. Cold does not kill, but a sufficiently high temperature destroys any germ. The exact point which proves destructive to viability is known as the *thermal death-point.* As moist and dry heat are not equally efficacious, each will have its own thermal death-point. Cultures in different media and of different ages often show marked differences in the temperature necessary to kill.

Chemic Disinfection.—In addition to the influence of thermic changes on bacteria, it is necessary to study the effect

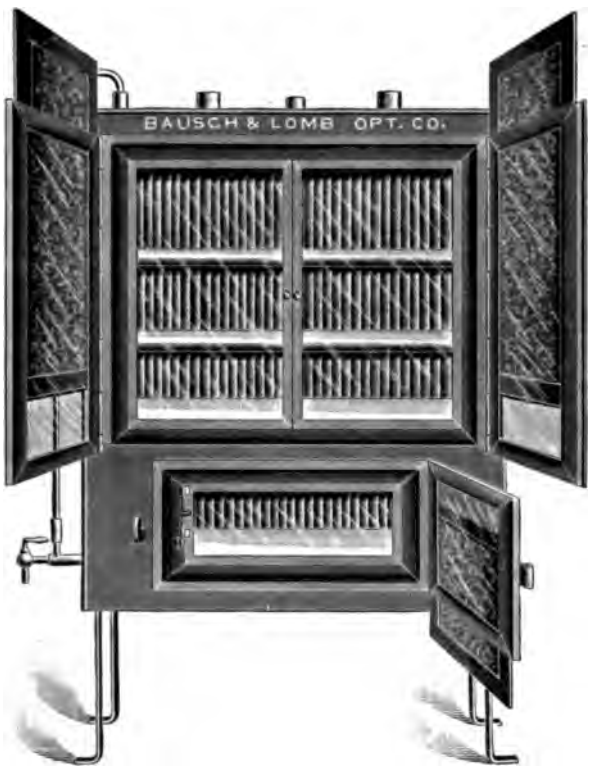


FIG. 167.—LARGE LABORATORY INCUBATOR.

Many bacteria grow at room temperature; a few, however, have but a slight range of temperature in which growth will occur; above or below this point growth ceases. For the cultivation of such organisms and for maintaining any culture at its optimum temperature an incubator is necessary. The above is a larger form than is needed for individual work; it serves, however, to illustrate the essential features of an incubator; double doors with sliding fronts, shelves, etc.

of disinfectants belonging to the chemic group. The relation of other physical agents than heat may also be studied,—*e. g.*, drying, light, and electricity. In studying disinfectants

we are to use solutions almost exclusively ; insoluble disinfectants are of more than doubtful value. Again, a culture medium must be used which does not alter the chemical in question. Thus, if, in the study of corrosive sublimate, a culture medium rich in albumin or strongly alkaline be used, the mercurial is instantly decomposed when it comes in contact with the culture medium, and, it may be, before it has had time to act upon the bacteria. Having found the desired culture

FIG. 168.—SMALL INCUBATOR SUFFICIENTLY LARGE FOR INDIVIDUAL WORK.

medium, the next point to determine is the exact point at which the body under investigation ceases to be antiseptic ; that is, inhibits the growth without of necessity destroying the life of the bacteria. For this purpose a series of tubes of culture media are prepared containing the antiseptic in varying quantities. These are best prepared, if possible, by taking 50 or 100 tubes of the medium it is desired to use, sterilized in the usual way : To ten of these enough of the

agent is added to make the strength ten per cent.; to another ten, enough to make the strength five per cent.; to another ten, four per cent., and so on, covering various percentages.

All these tubes are inoculated with the germ which it is proposed to use for the test. A series will be found beyond which the agent is in such dilution as not to interfere with the growth and above which the dilution may be antiseptic without, of necessity, destroying the germ,—inhibits growth but does not disinfect. The strength at which disinfection—that is, destruction of reproductive power—occurs, may be approximately inferred by diluting with the same sterile culture medium the tubes in which no growth has evinced itself so that the proportion of the disinfectant in the dilution shall be less than that already found to not inhibit growth. After this dilution the bacteria, which have not been destroyed, develop, showing in what strength disinfection has been complete. This has, however, taken so much time, probably days, that we may be still in doubt as to the rapidity with which the agent in question acts; and as the time required by a given solution to destroy viability is important, we must determine the rapidity of action and the strength necessary to use to be practically available. For this purpose a number of methods have been suggested, all of which are open to certain sources of error.

A number of cultures in a liquid medium have added to them the agent under study so as to make the percentage such as has been found in the previous test to be destructive; the added solution is thoroughly mixed with the culture from which inoculations are made at intervals of minutes for as long as an hour. The removal must be made into tubes containing sufficient of the medium to dilute the material carried over beyond the strength already shown to have an inhibitory action, so that any undestroyed bacteria may be free to develop.

The source of error by this method lies in the clumping

of the germs in the original tube; if grouped in clumps the agent may not have penetrated the clumps. Penetration is a most important point, for without this power a disinfectant is of little practical value; as, in all purposes for which germicides are used, a certain degree of penetration is necessary, so that this apparent objection is not without its good side. To get rid of the clumps, cultures are made in a medium containing fine quartz sand; this is shaken up in the culture and the culture filtered through glass wool and the filtrate used for the test. Tubes containing the sand may have mixed with them growing cultures containing no sand. Again, threads of silk two cm. to four cm. or six cm. in length may be placed in tubes of liquid culture media, the tubes sterilized as usual, and when sterile infected with the germ which it is intended to use for the test. When the culture is well grown it is shaken, the threads are withdrawn, and may be used as test-bodies to disinfect; they may be first dried in sterile dishes, or they may be used moist. A source of error lies in the quantity of the disinfectant which the thread may convey into the tube into which it is transplanted after treatment with the disinfectant. In some cases this may be partly avoided by washing the thread in sterile water, or in some solution; or exposing it to a vapor, which by chemic action converts the disinfectant into an insoluble or inactive compound. Thus, threads which have been in corrosive sublimate solutions may be exposed to ammonium sulphid vapor, the solution converting the mercurial into an insoluble and inactive sulphid.

It will be noted that one of the essential elements is to make the transplant, after treating the thread or culture with the disinfectant, into such a quantity of new non-infected medium as to assure a dilution beyond the inhibiting point, which may be due to any of the antiseptic carried over on the thread or on the platinum loop. Thus, if a thread has been

exposed to a solution of an agent, say in the strength of 1 : 100, and the inhibiting action is present in a solution having a strength of 1 : 1000, it will be necessary to carry the thread into a medium having a minimum bulk, in order to be safe, of at least 100 times the quantity carried over on the thread, in order to assure such dilution as to not preclude the disinfectant preventing growth of any undestroyed organism.

In testing, gases, threads, cultures, and other infected materials are exposed, in a closed chamber such as a bell-jar, to the gas either pure or with a known dilution of air.

In addition to the above system of tests, so-called *practical tests* are made. A known quantity of pus, blood, sputum, or feces is mixed with a known quantity of the disinfectant, and cultures made at intervals of from two to five minutes. Varying strengths of the disinfectant are used with exposure for varying lengths of time; in this way purely laboratory experiments are controlled by what are considered practical methods.

Again, animals may be inoculated with cultures or threads which have been exposed to disinfectants. In the latter case, it is to be remembered that in rare instances the pathogenicity may be reduced without the germ being destroyed.

Pathogenesis.—Koch has formulated, as conclusive evidence of the specificity of a given organism, the following requirements, which must be met :

(1) *The organism must be present in all cases of the disease.*

(2) *It must be cultivated in pure culture.*

(3) *It must produce the disease by inoculation in susceptible animals.*

(4) *From such animals the germ must be obtained and again cultivated in pure culture.*

To this cycle of proof has recently been added another demand for experimental evidence of pathogenicity :

(5) From cultures of the organism there should be demonstrated a toxin which, without the germ, will produce the

phenomena of the disease, or by means of which an antitoxin or immunizing substance can be developed in susceptible animals, lessening or removing their liability to the disease presumed to be produced by the organism in question.

Any evidence less conclusive than that afforded by the above requirements can be considered but presumptive knowledge of specificity. So many diseases occur in man and not in lower animals, that the best we can hope to do in such cases is to produce, by experiment or otherwise, as much of the proof as possible, and accept the germ as the cause in the absence of any equally or more rational conclusion. In some diseases—for example, leprosy—this is practically the stage at which the scientific inquiry at present rests.

To study the pathogenesis of an organism, **inoculation of animals** is necessary. The animals most used are the rabbit, guinea-pig, rats, and mice. The absolute requisite to success is careful asepsis at every stage of the process, and during the postmortem if the animal dies. If the disease or a disease is produced and it is desired to obtain cultures, they must be secured with the same strict attention to detail.

All instruments used in the various stages of inoculation, examination during life, or postmortem, should be sterilized by heat, preferably dry, although moist heat may be used. Chemic disinfection must be regarded with suspicion, although syringes may be sterilized in a five per cent. solution of carbolic acid allowed to act for one or, better, two hours, during which time it is kept warm. Pure formalin may be used on instruments. No matter what chemic body is used, it must be thoroughly removed by washing in sterile water before proceeding with the operation. The hands of the operator and assistants, and the table upon which the operation is to be conducted, should be washed with soap and water as hot as can be tolerated, followed by alcohol, ether, and finally corrosive sublimate solution (1 part of the

salt dissolved in 1000 parts of normal salt solution), which should be allowed to act several minutes, followed by thorough washing in sterile water.

Of the many methods for inoculating an animal, the following will be found useful:

(1) *Subcutaneous inoculation* is the one most frequently used. The seat of the contemplated operation is shaved, washed with soap and water, water, alcohol, ether, alcohol, and corrosive sublimate solution 1 : 1000, and the last removed by thorough washing with sterile water. Between the scapulæ or near the tail are the most convenient sites for inoculation, but any point where the tissues are lax will answer the purpose.

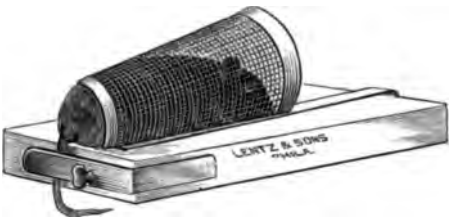


FIG. 169.—APPARATUS FOR HOLDING A MOUSE OR RAT FOR INOCULATION. (Devised by Dr. Lydia Rabinowitsch and Dr. Voges.)
The inoculation is usually made just over the root of the tail.

The skin is stretched and made tense, an incision or pocket is made in the tissues about five mm. to ten mm. in length and correspondingly deep under the skin; into the pocket so made a loop of the growing organism or suspected material is introduced, after which a layer of sterile cotton is laid over the wound and a thick coating of collodion applied; in a few minutes this will dry; the animal is then liberated and kept with an uninoculated animal known as the control.

(2) *Intraperitoneal injections* are made by preparing the animal as before. A syringe which is graduated into cubic centimeters is necessary for this method. The skin of the abdominal wall, the seat of the operation, is prepared as

previously explained, grasped by an attendant, and raised as a fold, into which the needle is introduced and forced onward into the peritoneum, then partly withdrawn to make sure it is free in the peritoneal cavity. The syringe is now attached, a given quantity of bouillon culture is introduced, and the wound sealed as before.

(3) *Intravenous inoculation* is made directly into the vein ; the most convenient veins are those of the rabbit's ear. The overlying skin is prepared as already directed, and an incision made down upon, but not into, the vein ; when the vein is thoroughly exposed, the needle of the hypodermic syringe is thrust into the vein in the line of the blood current, and the contents of

FIG. 170.—KOCH'S SYRINGE FOR HYPODERMIC, INTRAPERITONEAL, AND OTHER INJECTION METHODS FOR INOCULATING ANIMALS; THE CAPACITY SHOULD BE ABOUT TWO C.C.

the syringe slowly injected. Great care must be used to see that no air enters the vein, and that no clumps, or other solid material which might cause embolism, are thrown into the blood.

(4) *Inoculation Into the Anterior Chamber of the Eye.*—Anesthetize the cornea by cocain, wash with sterile water, perforate the cornea at the scleral margin with a hypodermic needle, through which the material is injected ; the quantity should be very small, scarcely a half drop, otherwise a disturbing tension is created which greatly modifies the result of the operation.

(5) *Tissue Implantation.*—Sometimes a small piece of patho-

logic tissue is used for inoculating (as in glanders and tuberculosis). The implantation may be made into the subcutaneous tissues or serous cavities. In the first instance, a pocket is prepared as already directed for subcutaneous inoculation, into which the block of tissue (which should not be larger than two mm. to five mm. cube,—the smaller the better) is implanted, the wound sealed, if necessary, sutured, and covered as already directed. For transplantation into a serous cavity, the peritoneum is usually selected. Under the strictest asepsis the cavity is opened, the tissue dropped in, and the opening closed. In some instances, in order to assure vascularization, a tip of the omentum is brought out, the block of tissue rolled in the serous membrane, and the roll secured by a stitch.

Aftertreatment of the Animal.—Medication of all kinds

FIG. 171.—SPATULA USED FOR SEARING THE SURFACE OF ORGANS BEFORE MAKING INCISIONS INTO THEIR INTERIOR FOR OBTAINING CULTURE MATERIAL.

should be avoided; overcome the immediate shock by the gentlest handling of the animal, abundance of fresh air, and warmth. It should be treated exactly as a control (an uninoculated animal of the same species), but, as a rule, should be in a cage or inclosure by itself, otherwise the control may injure the inoculated animal.

The Postmortem.—If the animal dies, the body should at once be washed with soap and water and water and alcohol, and immersed in 1 : 1000 corrosive sublimate solution, followed by washing with sterile water. With strict asepsis a postmortem is made. As soon as the heart is exposed, a spot on the surface of the right auricle is seared by heating a spatula and laying it down on the surface of the organ; this thoroughly disinfects the surface. Thrust a sterile inoculating needle into

the auricle, and move it through the blood backward and forward until a drop emerges along the side of the needle, when it is withdrawn and a tube of medium inoculated which may be at once poured into a plate. (See plate methods.) This operation is repeated for each cavity of the heart and for all important organs of the body. Pieces of tissue are hardened either in absolute alcohol or corrosive sublimate, and prepared for sections in the usual manner. (See Killing and Fixing of Tissues, p. 42, also Staining of Bacteria.)

BACTERIAL PRODUCTS.

As a result of the vital activity of bacteria we have elaborated certain substances, in addition to those already described, many of which are useful in preserving the species in its struggle for existence.

Tryptic enzymes are substances usually produced when certain organisms are cultivated in a nutrient medium containing albumin. They all liquefy gelatin, and a few will affect fibrin in the same manner. Enzymes do not dialyze. Enzymes are produced in greatest abundance when the organism becomes adapted to a special culture medium. The particular function of the enzyme seems to be an action whereby the pabulum of the bacteria is, in a sense, predigested.

Invertin is a peculiar substance elaborated by certain bacteria. Its principal function is converting, by a process of inversion, saccharose into dextrose and levulose. This process may be carried on either in the presence or absence of oxygen.

Various **acids** are produced by the specific action of bacteria. Among the most important are *lactic*, *acetic*, and *butyric* acids. The *bacillus acidi lactici* produces lactic acid from milk-sugar, and is considered the usual cause of acid fermentation in milk.

The mycoderma aceti (bacillus aceticus) produces acetic acid in dilute solutions of alcohol in the presence of oxygen. Butyric acid is produced by a large number of bacteria; the

FIG. 172.—BACILLUS BUTYRICUS. × 1000.

FIG. 173.—BACILLUS ACIDI LACTICI. × 1000.

most important one, however, is the bacillus butyricus, an anaërobic bacillus.

Putrefaction of animal and vegetable bodies is brought about by a great variety of bacteria. The products of this process are numerous, and are usually divided into two classes —the volatile and the non-volatile. The malodorous gases belonging to the former group are commonly the product of anaërobic bacteria.

Ptomains are basic substances containing nitrogen, and resemble in chemic constitution vegetable alkaloids. Many of these ptomains are toxic substances of the greatest potency, and, in contradistinction to others, of a harmless nature, are called toxins. Some of the most important toxins will be described:

Typhotoxin ($C_7H_{17}NO_2$). Brieger obtained this toxin from bouillon cultures of typhoid bacilli incubated for one week at a temperature of 37° C. The same observer asserts that the specific action of the bacillus typhosus is due to this toxin.

Tetanin ($C_{13}H_{30}N_2O_4$). Brieger separated this substance from impure cultures of the bacillus tetani grown in bouillon in an atmosphere of hydrogen. Tetanin, when injected into guinea-pigs, in rather large doses, induces a lethargic condition, shortly followed by increased rapidity of respiration and toxic and clonic spasms. Opisthotonos is also induced. *Tetano-*

toxin and *spasmotoxin* have also been obtained by Brieger from cultures of the bacillus of tetanus.

Cholin ($C_5H_{15}NO_2$). Obtained by Strecker from hog's bile, and by Brieger from various sources, including pure cultures of the spirillum of Asiatic cholera. Toxic only in large doses. Brieger has obtained two ptomains from cultures of Koch's cholera spirillum, which would seem to be the cause of the peculiar symptoms of cholera. When injected into animals, one induces cramps and muscular tremors, the other diarrhea and collapse.

Tyrotoxicon, obtained by Vaughan from cheese, milk, and ice-cream. Symptoms produced by the eating of substances containing this poison are vertigo, headache, nausea, vomiting, epigastric pain, purging and griping pains, cramps in lower extremities, and great prostration.

Toxalbumins are substances developed during the growth of certain pathogenic bacteria in the presence of albumin. Toxalbumins differ essentially in composition from ptomains. Most of them are soluble in water; they are precipitated by alcohol, and they dialyze. Sewell first obtained a toxic albumose from snake poison. Hankin, pursuing the same line of investigation, isolated another substance, similar in composition, from pure cultures of anthrax bacilli.

The experiments of Roux and Yersin seemed to point conclusively to the presence, in diphtheria cultures, of an exceedingly toxic agent which was not a ptomain. Later (1890), Brieger and Fränkel demonstrated this substance to be a toxic albumose; and they were the first to employ the term toxalbumin. Brieger and Fränkel have separated toxalbumins from cultures of typhoid bacilli, the micrococcus pyogenes aureus, and spirillum of cholera. A toxalbumin has also been obtained from culture of the bacillus tetani. G. and F. Klemperer have succeeded in obtaining a toxalbumin from cultures of Fränkel's micrococcus of pneumonia.

The active principle in Koch's "tuberculin" is a toxic albumin elaborated by the tubercle bacillus. The toxalbumin obtained from cultures of micrococcus pyogenes aureus, spirillum of cholera, and typhoid bacillus are slightly soluble in water. The toxalbumins of diphtheria, anthrax, tetanus, and pneumonia are freely soluble in water. The constitutional symptoms in the above-mentioned infectious diseases are, in all probability, due to the presence of a toxalbumin.

IMMUNITY.

It has long been a recognized fact that a person having suffered from an attack of certain infectious diseases is more or less refractory to subsequent infection by the specific organism of that disease.

The bias thus given to the scientific mind has led to the most interesting and important investigations, whereby it would seem that such dreaded diseases as tetanus, diphtheria, hydrophobia, and tuberculosis may, eventually, be of rare occurrence and easily dealt with.

As far back as the early years of the eighteenth century it was known in Europe that the Turks inoculated their children with small-pox matter, in the hope of bringing on a mild attack of the disease and thereby inducing an immunity. To Lady Mary Wortley Montague belongs the honor of first calling serious attention to this practice, in a letter addressed to her friends in England, and dated March 23, 1718. In this letter is described the inoculation of her young son with small-pox matter. Jenner's remarkable discovery of the immunity conferred by the cow-pox virus shortly followed.

Within recent years scientists interested in the study and development of bacteriology have been called upon to explain this phenomenon, and many hypotheses have been advanced. Klebs and Pasteur believed that, in a first attack, something in the system essential to the life of the organism became

exhausted, and the germ died. A recurrence of the disease wholly depended upon a renewal of this substance, and in the interim the person possessed an immunity to the disease. Chauveau, supported by many eminent bacteriologists, believed that the immunity depended upon the accumulation in the system of bacterial products, which, having arrived at a certain degree of concentration, are incompatible with germ life.

Grawitz explained the induction of immunity by assuming that in infectious diseases a conflict between the cells of the body and the germs of disease ensues immediately upon the introduction of the latter into the tissues. If the cells are victorious in the combat, they ever after should possess increased power of resistance to this particular germ, and, in fact, be able to destroy it immediately upon its entrance into the tissues.

Buchner promulgated an explanation which was a slight modification of Grawitz's hypothesis. He assumed that in every infection there is an inflammatory reaction at the point where the germs localize, and that an alteration in the cells is thereby induced which subsequently enables the cells of the economy to resist and destroy that particular germ.

Metschnikoff next advanced his now celebrated theory of phagocytosis. He believed that the ameboid cells of the body take into their substance the bacteria, just as they would a particle of foreign matter or article of food, and, appropriating a portion to their own use, throw off the remainder into the blood, to be carried to and excreted by the emunctories. Although many cells of the body are competent to perform the function of phagocytosis, the typic phagocytes are the polynuclear leukocytes.

However, the process of immunity is not to be wholly accounted for by any one of the explanations thus far advanced, but is probably a complex process, involving a number of elements.

Experimentally, it has been determined that we may induce

immunity, not only by inoculation with the specific germ, but also by the introduction of the germ products and the serum of immune animals.

The earliest experiments upon this subject were made with the anthrax bacillus. Greenfield found that by cultivating this bacillus through several successive generations on the aqueous humor from the eye of an ox, its virulence was gradually diminished up to the twelfth generation, where it was lost completely.

In 1881 Toussaint announced that he had obtained a fluid capable of immunizing animals to anthrax. When inoculated into susceptible animals it did not produce death, but the animals so treated were refractory to virulent bacilli. This fluid was obtained by collecting the blood of an animal dead from anthrax and then defibrinating it by whipping. Later he also subjected it to a temperature of 55° C., and obtained thereby a more reliable fluid. Pasteur cultivated anthrax bacilli at a temperature of from 42° C. to 43° C., and found that by the end of the sixth week they were no longer capable of producing the disease.

Previously virulent organisms cultivated twenty-four days at the above temperature, when injected into sheep produced only a mild febrile reaction. Sheep thus treated are quite refractory to virulent cultures, and complete immunity may be conferred by a second injection of bacilli which have been cultivated under the same conditions for twelve days.

In these experiments Pasteur also found that the spores of attenuated bacilli, transplanted in fresh culture media and subjected to conditions highly favorable to their growth, developed into bacilli possessing the same degree of attenuation as those from which they were derived.

In our country about this time sterilized cultures of the organism of hog cholera were being used with a certain degree of success to protect the animal against this disease.

Hankin separated from anthrax cultures an albumose of the

utmost potency. This substance injected into rabbits in doses of $\frac{2}{5000000}$ of their body weight produced death; frequently repeated doses of the $\frac{1}{10000000}$ of the body weight, however, rendered the animal immune to the most virulent cultures.

Sewall isolated an albumose from snake poison which in extremely small doses protected pigeons for a period of three months against seven times the dose of snake poison which ordinarily proves fatal.

Working upon these lines various investigators have rendered susceptible animals immune to glanders, fowl cholera, tetanus, hydrophobia, and diphtheria.

The recent experiments of Kitasato and Behring are, in all probability, destined to bring about almost a revolution in the treatment of disease. Their investigations into the nature and quality of the serum of animals rendered immune to tetanus and diphtheria, have introduced the question of serum therapy —the all-absorbing topic of the day. The efficiency of this serum is supposed to depend upon the presence in it of a substance capable of neutralizing the toxin of the bacilli. The substance, a supposed albumose, is called the antitoxin. The preparation of the diphtheria antitoxin is as follows:

As the bacilli develop their toxins most rapidly in the presence of a moist current of air, a flat-bottomed vessel with two lateral tubes is charged with bouillon containing two per cent. of peptone. After thorough sterilization, inoculate with fresh virulent cultures of the diphtheria bacillus. Incubate at 37° C. until development begins, and then force through the lateral tubes a current of moist air.* A sufficient abundance of toxin will be developed in from three to four weeks. Filter through a Pasteur-Chamberlain filter, preserve in well-stoppered bottles, and keep in a dark place. This filtrate in doses of 0.1

* The aëration of the flask is no longer practised, experience having shown that it is not demanded.

c.c. should kill a guinea-pig weighing 500 gm. in from forty-eight to sixty hours. For the purpose of immunizing animals, this fluid is in many cases too strong for the first injections, and should be diluted with one-fourth its volume of Gram's solution. Roux and Vaillard have determined that the toxin is much less dangerous when combined with iodin. A medium-sized rabbit should receive an injection of 0.5 c.c. The injection is repeated in a few days, and

FIG. 174.—STERNBERG'S FLASK, USED FOR COLLECTING FLUIDS, WATER, ETC., AND FOR HOLDING CULTURES IN LIQUID CULTURE MEDIA.

Before using, it is sterilized in the hot-air oven. To fill, the point is broken off, the bulb heated, thus expelling some of the contained air; the point is then thrust into the fluid, and, as the bulb cools, the fluid rises into it; when the desired quantity is drawn into the bulb, the point is sealed in a gas flame. Certain brands of antitoxin are now dispensed in bulbs similar to the above.

FIG. 175.—KITASATO'S FILTER.

The material to be filtered is placed in the upper bulb, which is connected with the central bougie of unglazed porcelain. The point of connection between the receiving chamber and the filter bougie is covered by a rubber cork, which fits very tightly into the neck of the flask. Through the lateral arm of the flask extending out to the right the air is exhausted from the interior. In this way filtration, ordinarily slow, may be accelerated by air pressure. The filter is mostly used for separating germs from their toxins.

thus continued for several weeks. With each successive injection the proportion of Gram's solution should be diminished, and the dose slightly increased until the pure toxin is reached. If during this time a loss in body weight becomes

manifest, the injections should be stopped, or there may be induced a fatal cachexia.

Dogs, sheep, goats, horses, and cows may by this procedure be rendered immune. The milk of immune animals may offer an important source of the antitoxin. The horse is easily immunized, and will supply large quantities of the antidiphtheric serum. Horses bear proportionately large doses better than other animals, and but a transient fever will succeed a dose of from two to five c.c. of the strong toxin.

Antitoxin is obtained from the animal by bleeding under the strictest conditions of asepsis, receiving, through a cannula into a sterile jar, flask, or other container, the blood, as already directed for the preparation of blood-serum for culture purposes. The obtained serum is preserved by the addition of trikresol, thymol, carbolic acid, camphor, etc. It should be sterile.

Behring was the first to propose a method for estimating the immunizing action of serum. His method consists in estimating the strength of a serum according to the amount necessary to render an animal of known weight immune to a certainly fatal volume of the toxin injected twelve hours after the serum. By this we mean that, if a serum has a strength of 1 : 1000, one gm. of the serum will render a guinea-pig weighing 1000 gm. immune, twelve hours later, to a dose of the toxin which otherwise would certainly prove fatal.

Ehrlich has also proposed a method for estimating the immunizing strength of serum. His immunizing unit is a serum antitoxin, $\frac{1}{10}$ of a c.c. of which is capable of neutralizing $\frac{9}{10}$ of a c.c. of toxin.

An animal receiving a dose of serum is rendered refractory to a corresponding dose of toxin subsequently injected. If a guinea-pig receives an injection of serum the $\frac{1}{100000}$ of its body weight, it will resist a dose of toxin which kills the control animal in five days. An animal receiving a dose of

serum the $\frac{1}{50000}$ of its body weight will resist an injection of bacilli which kills the control animal in forty-eight hours. When the toxin is first injected the quantity of serum necessary to counteract it becomes greater with the lapse of time.

DESCRIPTIVE BACTERIOLOGY.

Bacteria are microscopic unicellular organisms. By the earlier investigators they were thought to be animal cells, belonging to the class infusoria; but now they are universally recognized as of vegetable origin. Their classification has given rise to considerable controversy; some observers placing them among the algæ, others among the fungi. It is probably best to consider them a distinct genus.

From certain peculiarities it is possible to divide bacteria into three distinct species, which, according to Nägeli's nomenclature, are known as follows:

Mucorini, or mold fungi; saccharomycetes, or yeast fungi; schizomycetes, or fission fungi.

The mucorini and saccharomycetes play but a small part in the production of disease in man.

The **mucorini, hyphomycetes,** or **mold fungi,** as they are variously called, consist of branched, septate filaments, called hyphæ. The hyphæ frequently develop lateral filaments, which form an interlacing network called the mycelium. The mycelial hyphæ produce large mother-cells, known as sporangia, in which develop a number of small, spheric, highly refractive bodies, called spores.

The hyphæ segment by the cylindric cells of which they are composed, increasing in length and dividing by fission. Reproduction of mold fungi is dependent largely upon the redevelopment of the spores formed in the sporangia or conidia.

The mold fungi of interest to physicians belong to the ascomycetes, or those mold fungi which develop in their sporangia eight spores.

Oidium Lactis.—Mycelium formed of branched septate filaments. Conidia, oval or spheric in shape, develop at the extremity of the mycelium, or a lateral septum. The branched hyphæ consist of short cylindric cells, which vary slightly in thickness. On milk, bread-paste, potato, and other culture

FIG. 176.—FAVUS. FROM A MOUSE.—(*Coplin and Bevan.*) × 800 diameters.
a. Germinating tube from gelatin culture. *b*. Conidia. *c*. Formation of fruit. *d*. Mycelium threads with fructification.

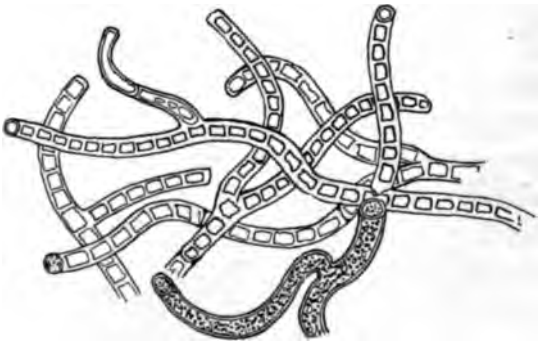


FIG. 177.—MICROSPORON FURFUR.—(*Coplin and Bevan.*) × 600 diameters.

media the oidium lactis forms a white growth. Stains with usual analin dyes.

The **Achorion Schönleinii (Favus), Trichophyton tonsurans (Herpes tonsurans), Microsporon furfur (Tinea versicolor)**, are considered by Grawitz as identical with the oidium lactis.

Aspergillus.—Grohe, by his investigation, was the first to show that certain varieties of the aspergillus were pathogenic for rabbits. Lichtheim's investigation demonstrated that the spores of the aspergillus flavescens and aspergillus fumigatus were actively pathogenic in rabbits. Grawitz also studied the pathogenesis of these molds, and confirmed Lichtheim's experiment. He also came to the conclusion that under certain conditions the penicillium glaucum acquires pathogenic properties—*e. g.*, when cultivated upon an alkaline medium, at temperatures of from 39° to 40° C.

The organism of **actinomycosis** is variously classified by different authorities, some placing it among the schizomycetes, others among the molds. Boström and Osler describe it as a cladothrix. For our purpose it may be classed with the mold fungi.

FIG. 178.—ACTINOMYCES (RAY FUNGUS). FROM BOVINE TUBERCULOSIS.—(*Coplin and Bevan.*) × 800 diameters.

Actinomyces, or **ray fungus,** is a polymorphous organism, being found in three distinct forms:

(1) Small spheric or coccus-like bodies 0.5 μ * in diameter. These bodies are supposed to be the spores.

(2) Filaments usually about 0.6 μ in breadth. The filaments sometimes appear as though formed by the juxtaposition of a number of small rod-like or spiral bodies. Many filaments do not show this seeming segmentation. The filaments frequently become closely interwoven; some may show branches or undergo dichotomous division.

(3) Club-forms, usually found in greater abundance than either of the other forms. They are regarded by Boström as degenerate structures or involution forms. Other observers,

* In the measurement of bacteria and similar small bodies, the micron or micromillimeter is taken as the unit. The micron, written μ, is $\frac{1}{1000}$ of a millimeter, or about $\frac{1}{25000}$ of an inch.

however, regard them as the true and essential reproductive structures of the organism, and claim to have discovered in them developing spores. The clubs are usually pyriform bodies composed of a limiting membrane with a clear, homogeneous, highly refractile protoplasm. They may be single or branched. They are disposed in a radiate manner about a center composed of fine granular matter. The center is prone to undergo calcareous infiltration.

In order to demonstrate the fungus in suspected material, usually pus, spread the matter over a glass plate and search carefully for yellow or yellowish-white grains which closely resemble granules of iodoform. The largest of these tufts will appear about the size of a pin's head. With a needle pick out one of these grains and transfer to a microscope slide and gently cover; examined with a low power, these grains are spheroid or globular, greenish in color, and quite opaque. While still in focus, with a needle make pressure on the cover-glass, focusing slowly downward; as soon as the mass falls to pieces, as it soon will do, under a higher power ($\frac{1}{12}$ in oil-immersion), the club-shaped masses become clearly defined. Staining is not necessary, but in sections or cover-glass spreads beautiful results may be obtained by the following: (1) Carbol-fuchsin, ten minutes gently warming the solution. (2) Rinse in water. (3) Saturated alcoholic solution of picric acid, five to ten minutes. (4) Water, five to ten minutes. (5) Fifty per cent. alcohol, fifteen minutes. (6) Dehydrate in absolute alcohol. (7) Clear in clove oil. (8) Mount in balsam. (Crookshank-Plaut.) Sections may also be stained in carbol-fuchsin, largely decolorized in 50 per cent. alcohol, washed in water, and stained in hematoxylin in the usual manner. From cultures, the fungus stains with most of the anilin dyes.

Pure cultures are obtained by plating: the grains are crushed in the nutrient gelatin and this spread as usual. In from four to seven days the colonies appear and are then inoculated on

agar-agar or gelatin. The agar-agar cultures are quite characteristic, the growth first appearing as a yellowish or yellowish-red dot, enlarging upon the surface of the culture medium as a scab-like mass with elevated and thickened edges, and as it becomes older gradually browning, resembling a dried blood scab, not uncommonly becoming black or brownish-black. Sometimes the culture medium turns brown. It grows fairly well at the ordinary room temperature, but best between 33° C. and 37° C.

Saccharomycetes, or Yeasts.—*Saccharomyces cerevisiæ*, the yeast used to make bread rise, offers a most suitable size for microscopic study. A small quantity of domestic yeast is shaken up with water and a drop of the mixture placed on a slide, covered with a clean cover-glass, and examined with $\frac{1}{6}$ or $\frac{1}{8}$ of an inch objective. The yeast cells are oval, round, or nearly spheroid, of varying sizes and slightly larger than a red blood-cell. Many of them will show buds and, if watched for a number of hours under the microscope with the slide kept warm, the buds can be seen form and separate, or may be seen clinging together. They may be cultivated on any of the ordinary culture media. As usually found, many cocci, bacilli, or even spiral forms are mixed with the yeast fungus, so that, when stained with the common laboratory stains, fields may be selected in which the yeast may be well compared with some of the fission fungi.

FIG. 179.—SACCHAROMYCETES CEREVISIÆ.—(*Coplin and Bevan.*) × 800 diameters.

Chromogenic Yeasts.—A number of yeasts have been isolated which, in cultures, produce color. Thus pink yeast, black yeast, red yeast, and a number of other forms have been described. In pure cultures these grow as already described, by budding, at the same time elaborating the color peculiar to each variety.

Saccharomycetes, or **yeast fungi**, are responsible for the

alcoholic fermentation in saccharin liquids. The yeast fungi multiply by gemmation, although some observers assert that the mycoderma forms ascospores. The only disease at present held to be attributable to yeast fungi is *thrush.*

Saccharomycetes Albicans, or *Oidium Albicans.*—Cells spheric or elliptic, .03 mm. to .05 mm. long, and .003 mm. to .005 mm. in diameter. They multiply by pullulation, and may produce mycelial-like filaments. The white patches which form on the mucous membrane of the mouth in thrush are produced by the saccharomyces albicans.

The **schizomycetes** form the most important group of the bacteria, and include all the important disease-producing germs.

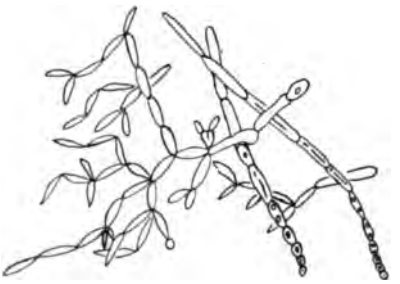


FIG. 180.—SACCHAROMYCETES ALBICANS (THRUSH FUNGUS).—(*Coplin and Bevan.*)

For convenience in study, we may subdivide the schizomycetes into three varieties according to morphologic peculiarities.

Schizomycetes: (I) Cocci; (II) Bacilli; (III) Spirilli.

(I) *Cocci.*—Spheric, slightly ovoid, or lancet-shaped bacteria, which reproduce by binary division, and occasionally by the formation of arthrospores.

The cocci form such complex varieties that a further subdivision will be necessary to facilitate our study of them:

By number { Monococci. Diplococci. Tetracocci. } By arrangement { Streptococci. Micrococci (staphylococci). Ascococci. Sarcinæ. }

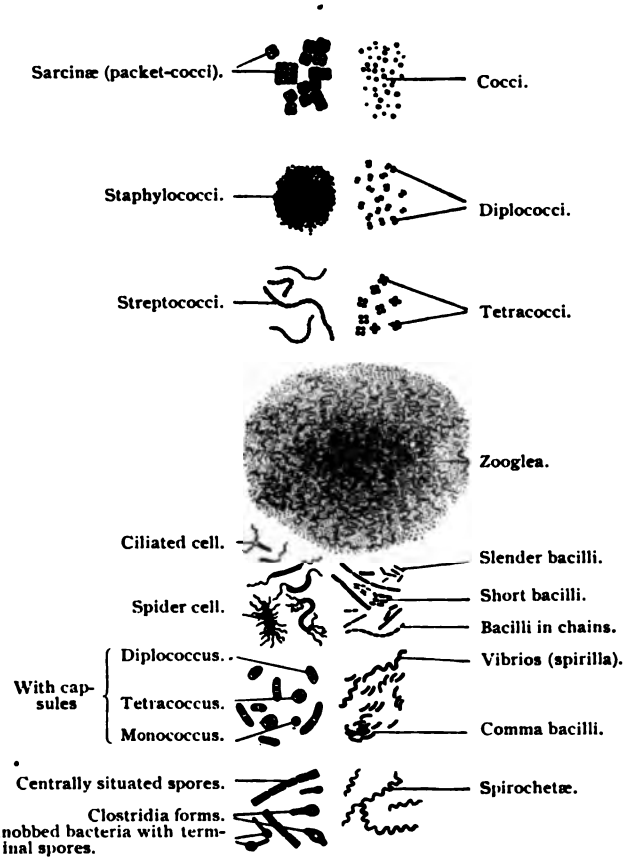


FIG. 181.—DIAGRAM ILLUSTRATING THE NOMENCLATURE OF SCHIZOMYCETES BASED UPON THEIR MORPHOLOGY.—(*After Schenk.*) × about 700 diameters.

Sarcinæ include the packet cocci: cocci arranged, in more or less cuboid shapes, as multiples of four. Each packet contains 8, 16, 32, or more units. The cocci proper include those named by the number commonly in the group, as: (*a*) Monococci, or cocci with no special arrangement or grouping; with these we include the staphylococci. (*b*) Diplococci, or cocci grouped in pairs. (*c*) Tetracocci, cocci grouped in fours. The second method of naming is by arrangement, as: (*A*) Streptococci, cocci arranged in chains; (*B*) ascococci, or encapsulated grouped cocci; (*C*) staphylococci, or cocci presumed to be arranged as grapes in a cluster. The student will fail to detect, under the microscope, the difference between the micrococci and the staphylococci. The term "zooglea" is applied to agminated masses of microbes, usually cocci, imbedded in a glue-like mass of gelatinous material elaborated by the microbe. The ciliated and spider cells are flagellate bacteria. The spirochetæ are flexible spirals, such as the organism of relapsing fever.

Varieties.—Diplococci: cocci associated in pairs. Tetracocci: cocci associated in fours. Monococci: cocci not definitely associated in any manner with one another. Streptococci: cocci arranged in such a manner as to form chains; the chains may contain 30 or more elements. Micrococci (staphylococci): cocci arranged in irregular masses; the individual elements are imbedded in a gelatin-like substance elaborated by the cocci. Ascococci: cocci associated in circular or globular masses (zooglea) held together by a gelatinous

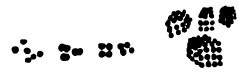


FIG. 182.—MONOCOCCI, DIPLOCOCCI, TETRACOCCI, AND SARCINÆ.—(*Coplin and Bevan.*)

FIG. 183.—ASCOCOCCI.

substance. Sarcinæ: cocci arranged in packets or cubes of eight or more elements.

(II) *Bacilli.*—Rod-shaped organisms, motile or non-motile, rigid or flexible. The organism formerly described as a bacterium is included in this class.

(III) *Spirilli.*—Curved or spiral filaments, rigid or flexible.

For recording the characteristics of an organism, the table on page 306 is introduced as illustrating what data should be worked out, and the usual sequence in which the results attained are recorded. The blank outlines, *b*, *c*, *d*, and *e*, have drawn upon them the appearances of the growing germ in cultures upon the media given.

TABLE ILLUSTRATING METHOD OF RECORDING THE PRINCIPAL CHARACTERISTICS OF AN ORGANISM.

(A) Where found.

(B) Morphology. (*a*) Form, (*b*) size, (*c*) arrangement.

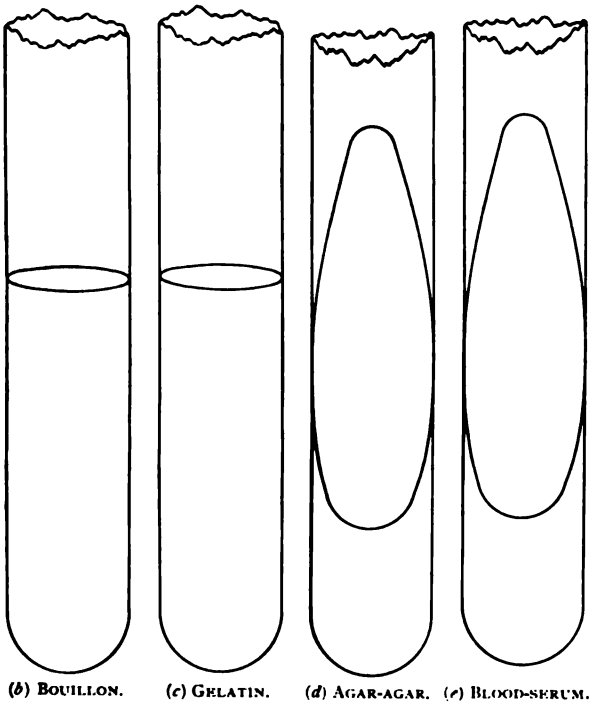
(C) Stains. Reaction to Gram's method of staining.

(D) Motility { (1) Flagellate. (2) Nonflagellate.

(E) Method of reproduction.

(F) Products of growth: (*a*) Acids, (*b*) alkalies, (*c*) odor, (*d*) color, (*e*) gases, (*f*) enzyme, (*g*) indol, (*h*) toxin, (*i*) toxalbumin, (*j*) other chemicobiologic reaction or product. MAKE DRAWING.

(G) Characters of growth on: (*a*) Plates,



(*b*) BOUILLON. (*c*) GELATIN. (*d*) AGAR-AGAR. (*e*) BLOOD-SERUM. (*f*) SPECIAL MEDIUM.

(H) (*a*) Aërobic, (*b*) anaërobic { (1) Facultative. (2) Obligate.

(I) Reaction of medium best adapted to its growth. Reaction of cultures in milk.

(J) (*a*) Optimum temperature, (*b*) thermal death-point { (1) Moist heat. (2) Dry heat.

(K) Influence of antiseptics and disinfectants.

(L) Pathogenesis.

(M) Immunity, method of securing, duration, blood characteristics in, and influence of blood-serum of immune animal on the organism.

(N) Remarks: Peculiarities not embraced in above.

SAPROPHYTIC BACTERIA.*

Bacillus Prodigiosus, also known as **Micrococcus Prodigiosus.**

Place Found.—In air, water, and on bread.

Form and Arrangement.—Rods; oval in shape, and about 1 μ in length; arranged singly and sometimes in groups.

Motility.—Motile.

Growth.—Grows profusely on all media. The growth is nearly blood-red. In bouillon it forms a ring upon the surface and clouds it; sometimes its pigment fades, and this can be brought back to a considerable extent by transplanting it on potato, upon which it grows exceedingly well. Liquefies gelatin.

Temperature.—Grows best at ordinary room temperature, although too high a temperature will destroy its pigment.

Aërobiosis.—Aërobic.

Reproduction.—By fission.

Pathogenesis.—Saprophyte.

Stains with gentian-violet, methylene-blue, carbol-fuchsin; also other anilin dyes. Stain for five to ten minutes; wash in water, dry in air, and mount.

* In addition to the yeasts and molds, the following non-pathogenic bacteria are introduced that the beginner may familiarize himself with methods before working with pathogenic forms. For this purpose various stains, hanging drop cultures, reaction, etc., should be studied. (See table, page 306.)

Bacillus Subtilis (Hay Bacillus).

Place Found.—In air, water, and hay infusions.

Form and Arrangement.—Rods; singly, in threads, and in irregular bunches. They are about 6 μ in length, and three times as long as broad. The ends are usually rounded.

Motility.—Motile.

Growth.—Grows on all the culture media. On agar-agar, a dirty white, wrinkled growth appears in from twelve to twenty-four hours. In bouillon it grows, first forming a pellicle, then precipitating to the bottom of the tube. Liquefies gelatin. Grows also on potato and blood-serum.

Temperature.—Ordinary room temperature.

Aërobiosis.—Aërobic.

Reproduction.—By fission and spores.

Pathogenesis.—Saprophytic.

Stains with carbol-fuchsin, gentian-violet, methylene-blue; also other anilin dyes. Stain for five to ten minutes, wash in water, dry in air, and mount. Stain for spores by methods already given. (See p. 267.)

PATHOGENIC BACTERIA.

Gonococcus, Neisser, 1879.

Place Found.—Within the cells of gonorrheal pus.

FIG. 184.—DIPLOCOCCUS OF GONORRHEA, GONOCOCCUS.—(*Coplin and Bevan.*) × 800 diameters.

Variety of Coccus.—Roll-shaped diplococcus; 0.8 to 1.6 μ in diameter.

Motility.—Non-motile.

Growth.—Human blood-serum; smooth, thin, grayish-yellow, moist film with ill-defined margins first develops; later, forms jagged protuberances with sharply-defined edges. Growth very slow. No growth on gelatin.

Temperature.—Optimum, 33° C. to 37° C. Maximum, 38° C. Minimum, 25° C.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis.—Produces gonorrheal inflammation when inoculated upon mucous membranes.

Make spread of the discharge on cover-slip ; dry and fix.

Stain with saturated alcoholic solution of methylene-blue for from five to fifteen minutes ; wash with water, and then stain with saturated alcoholic solution of eosin for the same length of time. Wash in water, dry, and mount. The nucleus of pus-corpuscles, as well as the gonococci, will be stained blue, while the protoplasm of pus-cells is stained pink with eosin. Does not stain by Gram's method.

Trachoma Coccus, Sattler, 1885.

Place Found.—Conjunctiva, follicles, and inclosed follicles of trachoma.

Variety of Coccus.—Roll-shaped diplococcus.

Motility.—Non-motile.

Growth.—May be cultivated upon gelatin, agar-agar, blood-serum, and potato. Forms a shining, light-gray film along the stab, or small globular colonies develop along the streak. Does not liquefy gelatin.

Temperature.—Optimum, 36° C.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis.—Pathogenic only in man. Inoculation in the conjunctiva followed by the development of typic trachoma.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin ; also other anilin dyes. Stain five to ten minutes ; wash in water, dry in air, and mount. Stains also by Gram's method.

Diplococcus Pneumoniæ, A. Fränkel, 1884.

Place Found.—In the sputum of those suffering from croupous pneumonia, severe cases of empyema, and exudate of cerebrospinal meningitis.

Variety of Coccus.—Diplococcus, lance-shaped. Usually

associated in pairs, end to end. Five or six may be arranged in the form of a short chain. In the exudates from the body they are found in capsules, which disappear when cultivated upon artificial media.

Motility.—Non-motile.

Growth.—Develops slowly and with difficulty upon gelatin. Usually forms small discrete colonies with sharply-defined edges and of a whitish color. Upon agar-agar delicate, shining, semitransparent colonies, which are almost invisible. Upon blood-serum a delicate, transparent, moist film. Non-liquefying.

FIG. 185.—DIAGRAM OF THE DIPLOCOCCUS OF PNEUMONIA, ILLUSTRATING RELATION OF CAPSULE TO THE CONTAINED GERM.—(*Coplin and Bevan.*)

Temperature.—Optimum, 35° C. Maximum, 42° C. Minimum, 24° C.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis. — Pathogenic in mice, guinea-pigs, and rabbits. In man the cause of croupous pneumonia.

Stains with carbol-fuchsin, gentian-violet, or methylene-blue; also other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount.

Friedländer recommends staining the pneumococcus in tissues as follows: Make a thin section of specimen, dissolve the paraffin from it, and stain for twenty-four hours in an acid solution of gentian-violet. This is made by taking 50 parts of a saturated alcoholic solution of gentian-violet, 100 parts of distilled water, and ten parts of acetic acid. After staining, decolorize with a one per cent. solution of acetic acid in water for one or two minutes, dehydrate with alcohol, clear with oil of cloves, and mount.

For *staining the capsule* of the pneumococcus a thin spread of sputum is obtained, dried, and fixed by passing it through the flame. It is next placed in a one per cent. acetic acid solution for a few minutes. The superfluous acid is now

drained off and the spread quickly dried in the air. Now place in a gentian-violet anilin-water for a few seconds. Wash in water, dry, and mount. The acetic acid removes a substance which is readily stained by the gentian-violet, thus leaving in the preparation, when finished, a pale background on which the brightly-stained capsules are readily detected.

Diplococcus Intercellularis Meningitidis, Weichselbaum, 1887.

Place Found.—In six cases of cerebrospinal meningitis, fresh exudate.

Variety of Coccus.—Usually found in pairs and fours.

Motility.—Non-motile.

Growth.—Does not grow upon gelatin. On tubes of agar-agar, with two per cent. gelatin, luxuriant growth appears upon the surface but penetrates the medium but little along the track of the needle. The growth is smooth, gray in color, and exceedingly viscid. Grows poorly upon blood-serum.

Temperature.—Develops only at about 36° C.

Aërobiosis.—Aërobic.

Reproduction.—Binary division. Maximum development in six days. Removals should be made every two or three days.

Pathogenesis.—Pathogenic in mice, rabbits, guinea-pigs, and dogs. Mice and rabbits especially susceptible, and die in from thirty-six to forty-eight hours after inoculation.

Stain.—Gentian-violet, methylene-blue, carbol-fuchsin; also other anilin dyes. Stain for five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method. Stains best with Löffler's methylene-blue.

Micrococcus * Pyogenes Aureus, Rosenbach.

Place Found.—Most frequent cause of suppuration. In

* The term staphylococcus is much used, particularly by surgeons, instead of micrococcus. The student should remember that the terms are interchangeable.

pus, draff, air, and earth. This organism, probably more nearly than any other, is ubiquitous.

Variety of Coccus.—Micrococci usually about 0.8 μ in diameter. Singly, in pairs, fours, and short chains of several elements, though most commonly in irregular masses.

Motility.—Non-motile.

Growth.—Tube cultures on gelatin. The growth after twenty-four hours appears as a faint white streak along the line of puncture. A deep yellow or golden pigment is gradually formed, and is well developed by the third day. The gelatin is liquefied and the organisms fall to the bottom, where they appear as a deep yellow precipitate. On tubes of agar-agar, the organisms develop along the stroke, forming a thin white or slightly yellow film, opaque and irregular in outline. Later the growth assumes the characteristic yellow color. The agar-agar frequently becomes cloudy and opaque. It is not liquefied.

FIG. 186.—MICROCOCCUS (STAPHYLOCOCCUS) PYOGENES AUREUS.—(*Coplin and Bevan.*) × 800 diameters.

On plates, the growth appears within from twenty-four to thirty-six hours as slightly-elevated colonies with sharply-defined edges. The colonies, white at first, later become a deep yellow or orange color.

Grows well on blood-serum. Same characteristics as when growing on agar-agar. On potato, white at first, later deep golden color; with age the growth becomes more succulent and develops a sour odor.

Temperature.—Optimum, 30° C. to 37° C.

Aërobiosis.—Facultative anaërobe.

Reproduction.—Binary division.

Pathogenesis.—When injected into the subcutaneous tissue produce abscess. Injected into the veins induce pyemia. Most common organism in suppurative processes.

Stains with gentian-violet, methylene-blue, carbol-fuchsin, and other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Stains very well in tissue by Gram's method.

Micrococcus Pyogenes Citreus, Passet.

In every respect it resembles the Micrococcus pyogenes aureus, except that it develops a lemon-yellow pigment.

Micrococcus Pyogenes Albus, Rosenbach.

Resembles the Micrococcus pyogenes aureus in every respect, except that it produces no pigment and the growth appears as a milk-white film.

Micrococcus Pyogenes Tenuis, Rosenbach.

Place Found.—In mild, though extensive, suppurative inflammations.

Variety of Coccus.—Irregularly-grouped masses and singly, 0.9 μ to 1 μ in diameter.

Motility.—Non-motile.

Growth.—On plates, appears as small, faint, transparent colonies, and upon agar-agar tubes as a thin, transparent, grayish streak along the inoculation stroke. The growth is very slow.

Temperature.—Probably grows best at body temperature.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis.—Negative results only have been obtained from the inoculation of animals.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount.

Micrococcus Cereus Albus, Passet.

Place Found.—In pus.

Variety of Coccus.—Micrococci, 1.16 μ in diameter. Usually grouped in irregular masses; may occur singly and in short chains.

Motility.—Non-motile.

Growth.—In gelatin plates, appear as small white colonies, seldom growing larger than the head of a large pin. In gelatin tubes the growth is almost wholly confined to the surface, and appears like a streak of wax with elevated irregular edges. The growth is quite rapid at a temperature of from 28° C. to 37° C. Does not liquefy the gelatin. On agar-agar it presents the same characteristics. Grows well on potato and blood-serum.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis.—Found in suppurative processes, but usually associated with one of the other pyogenic cocci.

Stains with gentian-violet, methylene-blue, carbol-fuchsin; also other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount.

Micrococcus Cereus Flavus, Passet.

Resembles the Micrococcus cereus albus, except that it develops a yellow pigment.

Streptococcus Pyogenes, Rosenbach and Passet.

Place Found.—Erysipelatous eruptions and pus.

Variety of Coccus.—Usually in long chains of from 20 to 30 or 40 elements (streptococci), 0.4 μ to 1 μ in diameter.

Motility.—Non-motile.

Growth.—Gelatin plates; small, circular, and finely-granular colonies, which, when fully developed, are light brown in color, edges slightly elevated, and center depressed. Does not liquefy the gelatin. In tubes of agar-agar small colonies develop on surface, especially along the inoculation stroke; later may form a thin, transparent film over surface. The growth is very slow. The organisms quickly lose their viability.

Temperature.—Optimum 35° C. to 37° C.

Aërobiosis.—Aërobic.

Reproduction.—Binary division.

Pathogenesis.—Produces erysipelas and also suppuration.

Stain with gentian-violet, methylene-blue, carbol-fuchsin; also other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount.

Streptococcus Erysipelatis, Fehleisen.

Probably identical with the former.

Micrococcus Tetragenus, Koch, Gaffky.

FIG. 187.—STREPTOCOCCUS OF ERYSIPELAS. —(*Coplin and Bevan.*) × 800 diameters.

Place Found.—In the sputum and cavities of tubercular pneumonia.

Form of Coccus.—Usually in fours, also in pairs. Tetracocci.

Motility.—Non-motile.

Growth.—Gelatin plates; small, white, finely-granular colonies having a vitreous luster. Grows well on agar-agar, potato, and blood-serum, forming a heavy white surface growth. The growth is slow at first, but after forty-eight or seventy-two hours more rapid. Does not liquefy gelatin.

Temperature.—Room temperature.

Aërobiosis.—Facultative aërobe.

Reproduction.—Binary division.

Pathogenesis.—Fatal to mice and guinea-pigs. Field-mice and rabbits refractory. Often found in man, associated with the Bacillus tuberculosis in tubercular pneumonia. To this disease, however, it bears no causal relation.

Stains with gentian-violet, methylene-blue, or carbol-fuchsin; also other anilin dyes. Stains very well by Gram's method, by which it can be demonstrated in tissue.

Bacillus Diphtheriæ, Löffler.

Place Found.—Diphtheric membrane.

Form and Arrangement.—Straight or slightly-curved rods, 2 μ to 4.8 μ in length, and 0.3 μ to 0.8 μ in breadth. The extremities usually stain with great intensity, while the center may remain clear, giving the organism a dumb-bell shape.

Motility.—Non-motile.

Growth.—In tubes of gelatin, small colonies developing along the puncture, and later becoming confluent, form a thin gray streak. Gelatin not liquefied. Blood-serum is best adapted to the cultivation of this bacillus, especially if it contains one per cent. of peptone, one per cent. grape-sugar, 0.5 per cent. sodium chlorid, and 25 per cent. of bouillon. Alkaline bouillon, milk, and agar-agar are culture media upon which they will grow. The cultures may retain their vitality for several months. A growth will develop upon potato; at first it is invisible, and only after several days does it appear as a dry, thin glaze.

Temperature.—Optimum, 37° C. Minimum, 20° C.

Aërobiosis.—Aërobe and facultative anaërobe.

Reproduction.—Entirely by fission. Spore formation does not occur.

Pathogenesis.—Inoculated on mucous membranes engenders a catarrhal, pseudomembranous, gangrenous, or other inflammation, associated with more or less systemic disturbance.

Stains with gentian-violet, carbol-fuchsin, methylene-blue; also other anilin dyes. Löffler's alkaline methylene-blue is specially adapted for staining it. Also stains well by Gram's method.

Bacillus Coli Communis, Emmerich.

Place Found.—In the intestinal tract of man and many of the lower animals.

Form and Arrangement.—Short rods, 1.6 μ to 3.2 μ in length, and 0.4 μ to 0.8 μ in breadth. At times they may assume an oval or spheric form. Usually arranged in irregular masses and in pairs.

Motility.—Motile.

Growth.—On gelatin plates colonies develop as small, flat, grayish points, with irregular outlines. In gelatin tubes the growth develops along the line of puncture as small, white,

globose colonies, and on the surface it spreads out as faint grayish film. The gelatin is not liquefied. Luxuriant growths develop on potatoes ; in color, slightly yellowish. On blood-serum a heavy growth quickly develops. An abundant growth will also develop on agar-agar. In many tubes gas will be produced in abundance. (See table, p. 327.)

Temperature.—Optimum, about 20° C. to 30° C.

Aërobiosis.—Aërobic and facultative anaërobe.

Reproduction.—Fission. Spore formation not observed.

Pathogenesis.—Small injections fatal to rabbits and guinea-pigs. When localized in the tissues engenders an intense inflammatory condition, and, according to some investigators, produces suppuration.

Stains with gentian-violet, carbol-fuchsin, methylene-blue, and other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

Bacillus Œdematis Maligni, Hesse, Koch.

Place Found.—Garden earth.

Form and Arrangement.—Rods from 3 μ to 5.3 μ in length and 1 μ to 1.1 μ in breadth. The ends are usually slightly rounded. Usually they are found joined end to end, though they may form chains of from 15 to 20 elements.

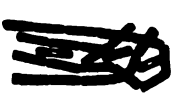


FIG. 188.—BACILLUS ŒDEMATIS MALIGNI. × 1000 diameters.

Motility.—Motile.

Growth.—On agar-agar plates opaque white colonies develop. Frequently they appear as shining, globose bodies with liquid contents. On agar-agar, containing two per cent. of grape-sugar, a profuse growth develops through the medium, imparting to it a diffuse cloudiness, most intense along the inoculation track. It grows also on gelatin, blood-serum, potato, and in guinea-pig bouillon. Liquefies gelatin.

Temperature.—Optimum, 37° C.

Aërobiosis.—Strictly an anaërobe.

Reproduction.—By fission and spore formation.

Pathogenesis.—Guinea-pigs and mice very susceptible. In man, produces extensive subcutaneous edema, beginning at the point of infection. Large quantities of gas are usually developed.

Stains with gentian-violet, methylene-blue, carbol-fuchsin, and other anilin dyes. (Stain for spores as described on p. 267.) Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

Bacillus Anthracis, Pollender and Davaine.

Place Found.—Blood of animals dying from splenic fever.

Form and Arrangement.—Rods varying greatly in size and having square ends. Length, 3 μ to 20 μ, breadth 1 μ to 1.25 μ. They are found singly, irregularly grouped, and in long threads of many elements.

FIG. 189. — BACILLUS ANTHRACIS.—(*Coplin and Bevan.*) × 800 diameters.

Composite field showing single bacilli, also a chain, and, above, a filament with spores. There are not uncommonly more than one spore to the bacillus.

Motility.—Non-motile.

Growth.—They grow quite rapidly upon agar-agar, gelatin, potato, blood-serum, and bouillon. A white growth develops quite rapidly along the line of inoculation, and from this point spreads over the surface of the media. Gelatin is liquefied, as is also blood-serum.

Temperature.—Optimum, 37° C. Minimum, 12° C. Maximum, 45° C.

Aërobiosis.—Aërobe.

Reproduction.—Fission and spore formation.

Pathogenesis.—The cause of wool-sorter's disease and malignant carbuncle in man. Cattle, horses, sheep, rabbits, and many other of the lower animals are susceptible to infection.

Stains with gentian-violet, carbol-fuchsin, and methylene-blue, as well as the other anilin dyes. (Stain for spores as described on p. 267.) Stain for from five to ten minutes;

wash in water, dry in air, and mount. Stains well in the tissues by Gram's method.

Bacillus of Symptomatic Anthrax, Feser and Bollinger.

Place Found.—In fluids and secretions of animals dying of symptomatic anthrax.

Form and Arrangement.—Fine rods, 3 μ to 5 μ in length, and from 0.5 μ to 0.6 μ in breadth, and with rounded ends. Found singly and in pairs, but rarely, if ever, in threads.

Motility.—Motile.

Growth.—Grows upon agar-agar, gelatin, blood-serum, potato, and bouillon. Colonies developing upon gelatin plates, appear at first somewhat spheric, with irregular outlines and granular surface. When the gelatin about them becomes liquefied they exhibit, by transmitted light, a thick, heavy center with radiating branches. On tubes of gelatin the growths become manifest in from twenty-four to twenty-eight hours. The color and general appearance is much the same as shown in plates. Considerable gas, having an acid, penetrating odor, is developed. The gelatin is liquefied.

FIG. 190.—BACILLUS OF SYMPTOMATIC ANTHRAX.—(*Coplin and Bevan.*) × 800 diameters.

Temperature.—Optimum, 37° C. to 40° C. Minimum, 13° C. Maximum, 70° C.

Aërobiosis.—Strict anaërobe.

Reproduction.—Spores and fission.

Pathogenesis.—The specific cause of symptomatic anthrax. Guinea-pigs very susceptible. Cattle, sheep, and goats susceptible. Cats, dogs, pigs, rabbits, pigeons, chickens, and ducks immune.

Stains with gentian-violet, carbol-fuchsin, methylene-blue, and other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method. (Stain for spores as described on p. 267.)

Bacillus Pneumoniæ, Friedländer (Friedländer's pneumococcus).

Place Found.—In lungs affected with croupous pneumonia.

Form and Arrangement.—Oval and short, thick rods. The oval organisms are often in pairs, with their ends in juxtaposition. When obtained from the lungs, usually incased in capsules.

Motility.—Non-motile.

Growth.—Grows well upon gelatin, agar-agar, blood-serum, and potato. On gelatin and agar-agar, in about twenty-four hours a slight grayish growth becomes visible along the inoculation streak. The gelatin becomes brownish, but is not liquefied. In a few days the growth takes on a peculiar glaze. Gas is formed.

Temperature.—Optimum, 28° C. Minimum, 14° C. Maximum, 34° C.

Aërobiosis.—Aërobe.

Reproduction.—Spore formation doubtful. Fission.

Pathogenesis.—May occasion a croupous inflammation in man. Mice, guinea-pigs, and dogs susceptible.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also the other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

Bacillus Pyogenes Fœtidus, Passet.

Place Found.—In fetid suppurative processes.

Form and Arrangement.—Short rods with rounded ends, singly and in short chains. Length, 1.45 μ and approximately 0.5 μ in breadth.

Motility.—Motile.

Growth.—Grows profusely upon gelatin, agar-agar, blood-serum, potato, and bouillon. In twenty-four hours a light gray streak becomes visible along the line of inoculation, from whence it spreads over the surface of the culture medium.

Gradually the growth assumes a brown hue, becomes thicker, opaque, and shining. Produces an exceedingly malodorous gas. Gelatin not liquefied. Growth very rapid.

Temperature.—Optimum, 30° C. to 37° C.

Aërobiosis.—Aërobe.

Reproduction.—Spores and fission.

Pathogenesis.—Pyogenic. Rapidly fatal to mice and guinea-pigs.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also the other anilin dyes. (Stain for spores as described on p. 267.) Stain for from five to ten minutes; wash in water, dry in air, and mount.

Bacillus Pyocyaneus, Gessard.

Place Found.—In green pus.

Form and Arrangement.—Short, delicate rods, 1.5 μ in length and 0.5 μ in breadth.

Motility.—Motile.

Growth.—Grows upon gelatin, agar-agar, potatoes, and milk. On solid media, a transparent film develops over the surface in about twenty-four hours. Later, it becomes a light gray or greenish color. The medium gradually becomes fluorescent. Gelatin is liquefied. Growth rapid.

Temperature.—Optimum 26° C. to 37° C.

Aërobiosis.—Aërobe.

Reproduction.—Fission.

Pathogenesis.—Pyogenic. In man, producing green pus. Fatal to guinea-pigs.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also the other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount.

Bacillus of Rhinoscleroma, von Frisch.

Place Found.—In nose of person suffering with rhinoscleroma.

Form and Arrangement.—Short rods with rounded ends

and oval elements. Found singly, in pairs, and in short chains. Commonly measures about 1.5 μ long and 0.5 μ broad.

Motility.—Non-motile.

Growth.—Grows upon gelatin, agar-agar, blood-serum, and potato. In tube culture, growth becomes visible in from twelve to twenty-four hours; first, as a milk-white film along the inoculation streak; later, spreads over surface of culture medium. Does not liquefy gelatin. Grows rapidly.

FIG. 191.—BACILLUS OF RHINOSCLEROMA. × 1400 diameters.

Temperature.—Optimum, 36° C. to 38° C.

Aërobiosis.—Facultative anaërobe.

Reproduction.—Spore formation doubtful. Fission.

Pathogenesis.—Specific cause of rhinoscleroma. Injected subcutaneously in mice, guinea-pigs, and rabbits, produces inflammation, suppuration, and death.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also the other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Stains well by Gram's method.

Bacillus Mallei, Löffler and Schultz.

Place Found.—In the nasal secretions and the nodules of glanders and farcy.

Form and Arrangement.—Rods 2 μ to 5 μ long and 0.5 μ to 1.4 μ broad.

FIG. 192.—BACILLUS MALLEI.—(*Coplin and Bevan.*) × 800 diameters.

Motility.—Motile.

Growth.—Grows well on all the common culture media, but especially so upon glycerin agar-agar. Develops as a pale, white, transparent film along the track of inoculation. Frequently such cultures show transverse striations.

Temperature.—Optimum, 37° C. On glycerin agar-agar grows at room temperature. Maximum, 43° C. Minimum, 25° C.

Aërobiosis.—Facultative anaërobe.

Reproduction.—Fission and spore formation.

Pathogenesis.—Specific cause of glanders. Man, horses, rabbits, guinea-pigs, and field-mice susceptible.

Stains with gentian-violet, methylene-blue, carbol-fuchsin; also the other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

Bacillus Tuberculosis, Koch.

Place Found.—In tubercular products and processes.

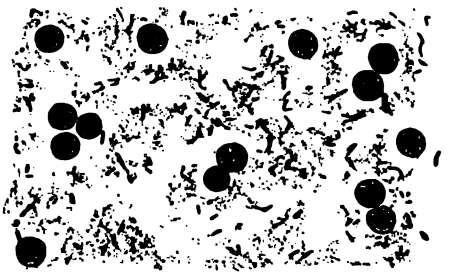


FIG. 193.—BACILLUS TUBERCULOSIS.—(*Von Jaksch.*) × 800 diameters.

Form and Arrangement.—Rods slightly curved or bent, ends rounded. Length, 1.5 μ to 3.5 μ; breadth, 0.25 μ.

Motility.—Non-motile.

Growth.—May be cultivated upon blood-serum and glycerin agar-agar. Upon blood-serum, small, transparent, light gray colonies first develop along the inoculation streak. Later, they become confluent, forming a grayish white growth. Upon glycerin agar-agar, small white colonies first develop; then, after a few days, coalescing, they form a uniform yellowish-white layer which is wrinkled or scale-like. The growth develops very slowly, requiring from two to three weeks to make its appearance on blood-serum, and from one to two weeks on glycerin agar-agar.

Temperature.—Optimum, 37.5° C. Minimum, 30° C. Maximum, 42° C.

Aërobiosis.—Aërobe.

Reproduction.—Fission. Spore formation probable, though involved in doubt.

Staining (*sputum*).—Search is made for yellowish, opaque, round particles, and when found a spread is made on a fine cover-glass by means of a platinum needle. The film of sputum thus obtained is allowed to dry in air, or is held high over a flame until dry. To coagulate the albumin and fix the specimen it is passed through a flame three times. It is then covered with carbol-fuchsin solution and heated for three minutes over an alcohol lamp or some distance above a Bunsen burner, not allowing the stain to boil or become dry. Wash in water, and apply a few drops of acid methyl-blue (Gabbett's counter-stain) for three minutes, or until all red color has disappeared. Wash in water and mount in water, or dry and mount in balsam, and examine with a $\frac{1}{5}$-inch objective. The tubercle bacilli appear as short red rods, while the ground, cellular elements and other bacteria are stained blue. When a hurried diagnosis is not required, the cover-glass spread can lie in carbol-fuchsin for twelve hours, without heating, and be counter-stained as just described. Specimens prepared in this way retain their color much longer, and when the organisms are not found by the rapid method, the slow stain should be tried.

Gabbett's Acid Methylene-Blue (counter-stain):

Methylene-blue, ...	2 parts	
Twenty-five per cent. aqueous solution of sulphuric acid, ...	100 parts.	M.

Ziehl-Neelson Method for Staining Tubercle Bacilli in Tissues.—Stain the section for fifteen minutes in carbol-fuchsin, which should be heated; decolorize in a 25 per cent. aqueous

solution of nitric or sulphuric acid; wash in 60 per cent. alcohol; for contrast, stain with methylene-blue; wash and dehydrate with alcohol. Clear with oil of cloves and mount in balsam. The tubercle bacilli will be stained red, and the tissues blue.

Bacillus Tetani, Nicolaier, Kitasato.

Place Found.—Earth. In the discharge from wounds of persons having tetanus.

Form and Arrangement. — Straight, slender rods with rounded ends.

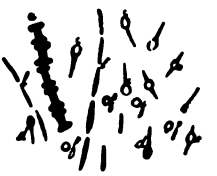


FIG. 194.—DIAGRAM ILLUSTRATING THE FORMS OF BACILLUS TETANI.—(*Coplin and Bevan.*)

a. Spool shape. *b.* Chain form. *c.* Clubbed bacilli, with spore at one end. *d.* Club without spore. *e.* Spindle form with spore in center. *f.* Free spores.

Motility.—Motile, except when spore bearing.

Growth.—Grows upon blood-serum, agar-agar, gelatin, and bouillon. The most favorable medium is nutrient gelatin having a slight alkaline reaction and containing one per cent. of grape-sugar. The growth becomes visible at the end of three or four days. In gelatin, stick culture colonies first make their appearance along the puncture below the surface. They usually coalesce, and form a branching or radiate growth. Gelatin is liquefied and a small amount of gas produced.

Temperature.—Optimum, 36° C. to 38° C. Minimum, 14° C. Maximum, about 42° C.

Aërobiosis.—Anaërobe and, after long cultivation, facultative aërobe.

Reproduction.—Fission and spore formation.

Pathogenesis.—The specific cause of tetanus. Man and many of the lower animals susceptible, especially guinea-pigs and rabbits.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also the other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Stains by

Gram's method. (Stain for spores as described upon p. 267.)

Bacillus Typhosus, Eberth, Gaffky.

Place Found.—Spleen and intestines of typhoid cadavers, feces, water.

Form and Arrangement.—Straight rods with rounded ends, 1μ to 3μ in length, 0.5μ to 0.8μ in breadth. Found singly, in irregular groups, and in cultures, forming long filaments.

Motility.—Motile.

Growth.—Grows upon gelatin, potato gelatin, agar-agar, potato, milk, and blood-serum. Upon agar-agar the growth is quite rapid. It first becomes visible along the line of inoculation as a grayish-white, semi-transparent film. Later on

FIG. 195.—BACILLUS TYPHOSUS, SHOWING FLAGELLA.—(*Gould.*) × 1200 diameters.

FIG. 196.—BACILLUS TYPHOSUS.—(*Coplin and Bevan.*) × 800 diameters.

it takes a yellow or brownish cast. The growth on an acid potato is significant; at first it is invisible, but imparts to the potato a moist, shining appearance by the development of a perfectly transparent film. The typhoid bacillus is non-liquefying.

Temperature.—Optimum, 36° C. to 38° C. Will grow at room temperature.

Aërobiosis.—Aërobe, facultative anaërobe.

Reproduction.—Fission.

Pathogenesis.—Specific cause of typhoid fever.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also with other anilin dyes. Stain for from five to ten minutes; the stain had best be warm; wash in

water, dry in air, and mount. Does not stain by Gram's method.

One of the most difficult differentiations which a bacteriologist may be called upon to make is between the Bacillus typhosus and Bacillus coli communis. The following tabulated points of difference is a modified and extended form of a table from Pearmain and Moor:

Media.	Bacillus Typhosus.	Bacillus Coli Communis.
Gelatin plates.	The colonies on the surface form large grayish-white expansions with irregular edges, and after a time become somewhat yellowish-brown. The depth colonies are darker, with regular edges. Under a low power the colonies exhibit a characteristic woven structure. The gelatin is not liquefied.	The colonies are round and oval, with smooth-rimmed margins. The surface colonies form dirty-white expansions, which on magnification exhibit a furrowed appearance. The colonies later become dirty yellowish-brown in color. The gelatin is not liquefied.
Gelatin streak culture.	Produces a grayish-white expansion with irregular edges. The growth has a tendency to keep to the inoculation streak, and often has a bluish iridescence.	Dirty yellowish-white expansion, which spreads all over the surface of the medium, and often has a bluish iridescence when viewed by transmitted light.
Gelatin shake culture.	No gas bubbles.	Copious formation.
Agar-agar streak culture.	Grayish-white expansion, which covers the surface of the medium.	Dirty yellowish-white expansion, which spreads over the surface of the medium.
Potatoes.	Generally a faint grayish-white growth; the growth varies, however, on different potatoes.	Slimy yellowish growth.
Milk.	Turns faintly acid. No coagulation takes place.	Curdled after one to three days.
Broth.	Rendered turbid, and gives no indol reaction.	Rendered turbid, and gives a well-marked indol reaction after from twenty-four to forty-eight hours.
Formalin broth (1 : 7000).	No growth.	Growth.

DIFFERENTIATING POINTS BETWEEN BACILLUS TYPHOSUS AND BACILLUS COLI COMMUNIS.—(*Continued.*)

MEDIA.	BACILLUS TYPHOSUS.	BACILLUS COLI COMMUNIS.
Elsner's differentiating medium.*	Growth rarely apparent under forty-eight hours. Colonies small, finely granular, shining, looking not unlike droplets of water.	Growth in twenty-four hours. Colonies large, coarsely granular, brownish, and more rapidly growing.
Widal reaction.	Positive reaction with blood-serum from a typhoid patient or an animal immunized against typhoid bacillus.	No reaction in either case.

Bacillus of Influenza, Pfeiffer, Canon.

Place Found.—In bronchial secretion and blood of persons suffering from influenza.

Form and Arrangement.—Small rods, 0.5 μ to 0.8 μ in length, and 0.2 μ in breadth.

FIG. 197.—BACILLUS OF INFLUENZA. × 1000 diameters.

Motility.—Non-motile.

Growth.—Grows upon glycerin agar-agar and bouillon. Upon glycerin agar-agar small, transparent, colorless colonies develop in twelve hours. The peculiarity of this growth is that the colonies always remain discrete, and only become visible with the aid of a lens. If 1.5 per cent. of sugar be added to the agar-agar, the colonies appear as small drops of clear water.

* Elsner's differentiating medium:

Selected potato, thoroughly cleaned, ... 0.5 gm.
Water, ... 1.0 liter.

Boil thoroughly, mashing the potato that the salts may be extracted and a part of the starch dissolved. Sufficient gelatin is added to render the medium solid, usually ten per cent.; after solution, sodium hydroxid is added until the reaction is but *faintly acid*, using litmus as the indicator; clarify, filter, and prepare as usual. To this medium one per cent. of iodid of potassium is added. The plates are made in the usual way.

Original article; *Zeitschr. f. Hyg.*, Bd. XXI., 1.

Temperature.—Optimum, 36° C. to 38° C. Does not grow below 28° C.

Aërobiosis.—Aërobe.

Reproduction.—Fission. Spore formation not observed.

Pathogenesis.—Specific cause of influenza. Men, apes, and rabbits very susceptible.

Stains with carbol-fuchsin and Löffler's alkaline methylene-blue. Stain for from five to ten minutes; wash in water, dry in air, and mount. The bacillus manifests a peculiar end-staining or polar-detail staining, thereby often appearing as a diplococcus. They stain also with ordinary anilin dyes, but do not stain by Gram's method.

Bacillus of Bubonic Plague.

Place Found.—In the blood of patients suffering from the disease; also in the urine.

Form and Arrangement.—Small spindle-shaped bacilli, arranged in sharply and repeatedly bent chains; also long and short forms, with intermediate stages.

Motility.—Non-motile.

Growth.—On agar-agar and in bouillon forms characteristic growths. In bouillon the growth should not be disturbed, but placed on a perfectly steady shelf; twenty-four to forty-eight hours after inoculation flakes appear underneath the surface, forming small islands of growth (Haffkine). The best medium is an alkaline solution of peptone, containing one or two per cent. gelatin. It causes acid formation.

Temperature.—Optimum 37° C.

Aërobiosis.—Aërobe and facultative anaërobe.

Reproduction.—By fission.

Pathogenesis.—Pathogenic in man, small laboratory animals, as rats, guinea-pigs, and rabbits; pigeons are exempt.

Stains with carbol-fuchsin, gentian-violet, methylene-blue, and other anilin dyes. Stain for from five to ten minutes; wash

in water, dry in air, and mount. Does not stain by Gram's method.

BACILLI NOT CULTIVATED OUTSIDE THE BODY.

Bacillus Lepræ.

Place Found.—In leprous lesions.

Form and Arrangement.—Rods resembling the tubercle bacillus. Usually, they are from 4 μ to 6 μ in length and 0.6 μ in breadth.

Motility.—Non-motile.

Growth.—Bordoni-Uffreduzzi has obtained growths of what he believes to be the lepra bacillus upon blood-serum containing peptone and glycerin. The India Leprosy Commission claim to have obtained cultures of the lepra bacillus upon blister-serum. As the organism cultivated by Bordoni-Uffreduzzi greatly differs from the lepra bacillus in leprous lesions, in both size and shape, its specific character may be doubted.

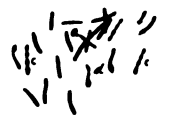


FIG. 198.—BACILLUS OF LEPROSY.—(*Coplin and Bevan.*) × 800 diameters.

a. Mature bacilli. *b*, *c*. Beaded bacilli. *d*. Slightly curved forms.

Reproduction.—Fission and possibly spore formation.

Pathogenesis.—Specific cause of leprosy in man. Rabbits are susceptible to infection, and usually die in several months from a general infection.

Stain.—Like the tubercle bacillus, the Bacillus lepræ stains with difficulty, but, once stained, retains the stain, so that, as in tuberculosis, the differentiation from other organisms is largely effected by bleaching one stain out of them, as carbol-fuchsin, and after-staining with a second stain, as methylene-blue, the bacillus of leprosy retaining the first stain and associated bacteria the other.

Stains with gentian-violet, carbol-fuchsin, methylene-blue; also with other anilin dyes. Stain for from five to ten

minutes in hot stain, or several hours in cold solutions; wash in water, dry in air, and mount. Stains in the tissues by Gram's method.

Bacillus of Syphilis, Lustgarten.

Place Found.—Syphilitic secretions and lesions.

Form and Arrangement.—Straight and curved rods resembling the tubercle bacillus. Their outlines are irregular and their ends bulging.

Reproduction.—Fission. Spore formation probable.

FIG. 199.—BACILLUS SYPHILIDIS.—(*Lustgarten.*) × 1000.

Pathogenesis.—Claimed by Lustgarten to be the specific cause of syphilis.

Growth.—Has not been successfully cultivated.

Stain.—Tissues are stained as follows (Lustgarten's method): (1) Anilin-water-gentian-violet, twelve to twenty-four hours; (2) wash in alcohol, two to three minutes; (3) aqueous solution potassium permanganate (½ per cent.), ten seconds; (4) aqueous solution sulphuric acid, two seconds; (5) aqua destillata. Repeat the last three directions until the section is colorless. Wash in alcohol, clear in oil of cloves, and mount.

SPIRILLI CULTIVATED OUTSIDE THE BODY.

Spirillum of Finkler and Prior.

Place Found.—Intestinal canal and dejecta from patients with cholera nostras.

Form and Arrangement.—Curved rods from 0.6 μ to 2.5 μ in length, 0.5 μ to 0.6 μ in breadth; resembles the spirillum of Asiatic cholera, but the "commas" are longer and thicker and not so uniform in diameter, the central portion being thicker than the pointed ends. The spiral filaments are not numerous, and are usually short.

Motility.—Motile.

Growth.—Grows on agar-agar, gelatin, blood-serum, potato, and bouillon. On agar-agar a moist, slimy layer is quickly developed. On gelatin plates, at the end of twenty-four hours, small, white punctiform colonies are seen, which cause a rapid liquefaction of the gelatin. In gelatin stick cultures, the liquefaction progresses rapidly, at the end of forty-eight hours assuming the shape of an old stocking. On blood-serum the growth is rapid, and causes liquefaction of the medium. On potato it produces a slimy, grayish-yellow, glistening layer.

Temperature.—Ordinary room temperature.

Aërobiosis.—Aërobe and facultative anaërobe.

Reproduction.—By fission.

Pathogenesis.—Pathogenic for guinea-pigs when injected into the stomach by Koch's method.

Stains with carbol-fuchsin, methylene-blue, and gentian-violet; also with the other anilin dyes. Stain for from five to fifteen minutes; wash in water, dry in air, and mount.

Spirillum Tyrogenum, Deneke.

Place Found.—Old cheese.

Form and Arrangement.—Curved rods and long, spiral filaments resembling spirilla of Asiatic cholera. The diameter of the commas is uniform throughout. The turns in the spiral filaments are longer and closer together, and the diameter of the curved segments less than those of the cholera spirillum.

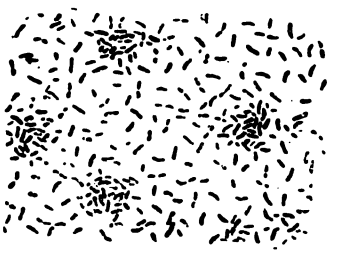


FIG. 200.—SPIRILLUM TYROGENUM.—(*Prof. von Jaksch.*) × 900 diameters.

Motility.—Motile.

Growth.—On agar-agar, gelatin, potato, and bouillon. On agar-agar thin yellowish layer forms along the inoculation streak. On gelatin plates small, yellow, punctiform colonies are developed, which have a sharp outline, but when liquefaction commences the sharp outline disappears. In gelatin stick

cultures liquefaction occurs along the whole line of puncture, the spirilla sink to the bottom as a coiled mass, while a thin yellowish layer forms upon the surface. On potato a yellow layer is usually developed.

Temperature.—Ordinary room temperature.

Aërobiosis.—Aërobe and facultative anaërobe.

Reproduction.—By fission.

Pathogenesis.—Pathogenic for guinea-pigs when injected into the stomach by Koch's method.

Stains with carbol-fuchsin, methylene-blue, gentian-violet; also with other anilin dyes. Stain from five to fifteen minutes; wash in water, dry in air, and mount.

Spirillum of Asiatic Cholera, Koch.

Place Found.—In the intestinal canal and feces of cholera patients.

Form and Arrangement.—

FIG. 201.—SPIRILLUM OF CHOLERA.—(*Coplin and Bevan.*)

A diagram illustrating the formation of comma-shaped segments from the breaking up of spiral forms.

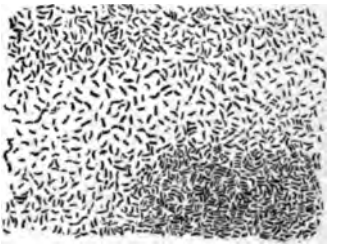


FIG. 202.—SPIRILLUM OF ASIATIC CHOLERA.—(*Prof. von Jaksch.*) × 900 diameters.

Short, comma-like elements; also U and S forms and long spiral filaments.

Motility.—Motile.

Growth.—Grows upon gelatin, agar-agar, blood-serum (which it liquefies), potato, and bouillon. The growth on gelatin is most characteristic. In stab cultures the growth begins at the surface and proceeds along the line of puncture. Liquefaction begins at the surface and accompanies the

growth. The growth presents a funnel-like appearance, and an air-bubble is usually observed in the broad, expanding portion of the funnel.

Temperature.—Optimum, 37° C. Minimum, 14° C. Maximum, 42° C.

Aërobiosis.—Aërobe, facultative anaërobe.

Reproduction.—Fission and spore formation (arthrospores).

Pathogenesis.—Specific cause of Asiatic cholera in man. Asiatic cholera has been experimentally produced in guinea-pigs with this spirillum.

Stains best with gentian-violet and carbol-fuchsin; also other anilin dyes may be used. Stain for from five to ten minutes, except with carbol-fuchsin, which should be left on for from fifteen to twenty minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

SPIRILLUM NOT CULTIVATED OUTSIDE THE BODY.

Spirillum of Relapsing Fever, Obermeier.

Place Found.—In the blood of relapsing fever patients during the fever paroxysms.

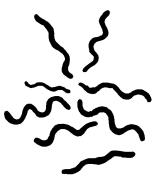


FIG. 203.—SPIRILLUM OF RELAPSING FEVER (SPIROCHÆTA OBERMEIERI).—(*Coplin and Bevan.*) × 800 diameters.

Form and Arrangement.—Delicate, flexible, spiral, or wave-like filaments, with pointed ends. Their length is from 40 μ to 60 μ, and their breadth about 0.1 μ.

Motility.—Very actively motile.

Reproduction.—Fission. Although spore formation has not been demonstrated, it probably occurs.

Pathogenesis.—Specific cause in man of relapsing fever. Monkeys are susceptible.

Stains with gentian-violet, methylene-blue, and carbol-fuchsin; also other anilin dyes. Stain for from five to ten minutes; wash in water, dry in air, and mount. Does not stain by Gram's method.

QUESTIONS.

(1) What is a culture medium? (2) Give classification of culture media. (3) Give example of each. (4) Describe the preparation of blood-serum. (5) How sterilize blood-serum (*a*) to retain it as a liquid medium? (*b*) to convert it into a solid medium? (6) What is Löffler's medium, and for what organism is it mostly used? (7) How is milk prepared for culture purposes? (8) In what way may it be a test-medium? (9) How prepare a potato for culture purposes? (10) How prepare Koch's alkaline-beef-peptone-bouillon? (11) Describe the preparation of beef-peptone-gelatin. (12) What precautions are necessary to assure alkalinity of the medium? (13) How is it clarified? (14) What is agar-agar? (15) How is beef-peptone-agar prepared? (16) What advantages has agar-agar over gelatin? (17) What are culture containers, and which are most used? (18) How cleanse them? (19) What is used to stopper the container, and why? (20) How sterilize them? (21) How fill test-tubes and sterilize the charged tubes? (22) Describe the Arnold steam sterilizer. (23) Describe the autoclave. (24) Can gelatin or blood-serum be sterilized in the autoclave? (25) What is a pure culture? (26) What is the object of plating, and upon what basis is it conducted? (27) Describe bottle plating. (28) Describe Petri dish plates. (29) How are plates made by Esmarch method? (30) What is the subsequent treatment of plates? (31) How transplant from culture to culture or from plate to culture tube? (32) What is meant by (*a*) streak or stroke culture, (*b*) smear culture, (*c*) stab or thrust culture? (33) What is an inoculating needle? (34) How prepare stains for bacteria? (35) What dyes are most used? (36) How keep stock solution? (37) What is the Koch-Ehrlich anilin-water stain, and how is it prepared? (38) How is Löffler's alkaline methyl-blue prepared? (39) How prepare Ziehl's carbol-fuchsin? (40) How prepare a cover-glass film or spread for staining? (41) How is it to be fixed? (42) Give method of staining and mounting. (43) Describe Weigert's method of staining bacteria in sections. (44) Describe Gram's method. (45) Describe Neisser's method of staining spores. (46) Describe Löffler's method of staining flagella. (47) Describe Pitfield's method. (48) What are bacteria? (49) Into what general groups are they divided? (50) What are the mold fungi? (51) Give their method of growth, morphology, and how is reproduction carried on? (52) Describe the Oidium lactis. (53) Describe the Achorion Schönleinii. (54) Where is the ray fungus found? (55) Describe its forms. (56) How demonstrate the fungus in suspected material? how is it stained? (57) Describe its appearance in pure culture. (58) What are the saccharomycetes, and how is reproduction carried on? (59) What substances are

produced by growing yeasts? (60) How study gas production by bacteria? (61) Describe the Saccharomyces albicans. (62) What disease does it produce? (63) How are the schizomycetes subdivided? (64) What is a coccus? (65) Give subdivisions of cocci. (66) What is a bacillus? (67) What is a spirillum? (68) How do the schizomycetes multiply? (69) Describe spore formation. (70) What is meant by (*a*) chromogenic, (*b*) zymogenic, (*c*) pathogenic? (71) What is meant by aërobiosis and anaërobiosis? (72) How is locomotion assured? (73) How do we study motility? (74) Describe the drop-culture method in detail. (75) What is meant by the terms liquefying and non-liquefying? (76) How is milk a test-culture medium? (77) Describe the method for determining whether a given germ produces an alkali or an acid. (78) What is the "indol reaction" and how is the test made? (79) What is meant by the thermal death-point? (80) Describe the method of testing a disinfectant. (81) Give rules for tests to which an organism must respond in order to be demonstrated to be pathogenic. (82) Give preparation of instruments for experiments on animals. (83) How should the operator prepare himself? (84) How prepare the animal? (85) What are the common inoculation methods? and describe each. (86) Give aftertreatment of animal. (87) How make postmortem on an animal and isolate any bacteria which may be the cause of death? (88) What is meant by bacterial products? (89) What are tryptic enzymes? (90) What is invertin? (91) Name bacteria which produce acids. (92) What are ptomains? (93) From what are the following obtained: Typhotoxin; tetanin; cholin; tyrotoxicon? (94) What is a toxalbumin? (95) Name sources of some toxalbumins. (96) What is meant by toxin? (97) Describe the preparation of a toxin, giving an example. (98) What is an antitoxin? how is it produced? give an example. (99) How is the strength of an antitoxin estimated? (100) Give characteristics of the hay bacillus.* (101) Bacillus prodigiosus. (102) Gonococci. (103) Trachoma coccus. (104) Diplococcus of pneumonia. (105) Diplococcus intercellularis meningitidis. (106) Micrococcus pyogenes aureus. (107) What term is used instead of micrococcus? (108) Micrococcus pyogenes citreus. (109) Micrococcus pyogenes albus. (110) Micrococcus pyogenes tenuis. (111) Micrococcus cereus albus. (112) Micrococcus cereus flavus. (113) Streptococcus pyogenes. (114) Streptococcus erysipelatis. (115) Micrococcus tetragenus. (116) Bacillus diphtheriæ.

* This question implies a description of its morphology, where found, motility, temperature at which it grows, aërobiosis, reproduction, cultural peculiarities, pathogenesis, and staining. For sake of space the first part will be left out in the questions which follow.

(117) Bacillus coli communis. (118) Bacillus œdematis maligni. (119) Bacillus anthracis. (120) Bacillus of symptomatic anthrax. (121) Bacillus of pneumonia. (122) Bacillus pyogenes fœtidus. (123) Bacillus pyocyaneus. (124) Bacillus of rhinoscleroma. (125) Bacillus mallei. (126) Bacillus tuberculosis. (127) Bacillus tetani. (128) Bacillus typhosus. (129) Bacillus of influenza. (130) Bacillus of bubonic plague. (131) Bacillus lepræ. (132) Bacillus of syphilis. (133) Spirillum of cholera nostras. (134) Spirillum tyrogenum. (135) Spirillum of Asiatic cholera. (136) Spirillum of relapsing fever. (137) Give, in order, all the data to be worked out in describing in detail the characteristics of an organism. (See table, p. 306.)

CHAPTER IX.

ANIMAL PARASITES.

Sporozoa, psorosperms (gregarinidia) are animal parasites belonging to the protozoa. In the lower animals a number of diseases are produced by members of this group; coccidial disease of the liver in rabbits affords an opportunity to study the **Coccidium oviforme** to which the disease is due. A similar cystic lesion occurs in the liver of man, the cysts containing coccidia. Coccidia are oval, long diameter 18 μ to 25 μ, with nuclei grouped in the center. Occasionally the coccidial masses resemble tubercles, solid, fibrous, or caseous areas. While most common in the liver, the spleen, kidney, and ureter may be involved.

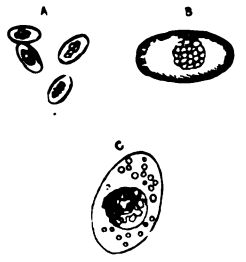


FIG. 204.—COCCIDIUM OVIFORME FROM THE HUMAN LIVER.—(*After Leuckart.—Gould.*)
A. × 200 diameters. B, C. × 800 diameters.

Keratosis folliculosis and Paget's disease of the nipple are conceded to be due to psorosperms. Paget's disease was long looked upon as an eczema, and was noted to eventually terminate in cancer of the breast. Russell described bodies thought to be psorosperms in cancer, but the demonstration was not complete.

Cercomonas intestinalis, length 10 μ to 12 μ, pear-shaped, with two terminal filaments, one of which is rigid, the other motile, by the action of which the parasite moves. In addition to the terminal filaments there are three tentacles on each side. The parasite is found in the stools during life and

in the intestine postmortem. There seems to be necessary a diseased condition of the intestinal mucosa before this parasite will thrive in the intestine, but when once present it induces diarrhea.

Closely resembling the preceding is the **Trichomonas intestinalis,** which differs in having a disc anteriorly supplied with cilia.

Amebæ belong to the rhizopodia. A number of forms have been described, the most important of which seems to be the **Amœba coli,** associated with dysentery and hepatic abscess. As seen in stools, amebæ are oval in outline, 20 μ to 35 μ in diameter; while living and in the fresh state, motile. The nucleus is round, with granular perinuclear protoplasm, which often contains vacuoles and included blood-cells, pus-cells, bacteria, and granules.

Flukes.—Certain forms of these are common in sheep. In man they infest the alimentary canal, or wander into ducts or canals which empty into it. The liver flukes, **Distoma lanceolatum,** seven to ten mm. in length, 1.85 to 2.25 mm. wide; **Distoma hepaticum,** 20 to 32 mm. in length, 8 to 20 mm. wide; **Distoma crassum,** five cm. in length, and the forms apparently so abundant in Japan, the **Distoma endemicum** and **Distoma perniciosum,** infest the duodenum and jejunum or invade the bile passages, producing cholangitis, jaundice, hepatic enlargement, and sometimes ascites. The irritation is not uncommonly associated with bacterial infection which eventually proves fatal.

A form of hematuria—**endemic hematuria** of Egypt—is due to the **blood fluke, Bilharzia hæmatobia.** The female is from 15 to 20 mm. in length and 0.7 mm. in diameter, and inhabits the portal vein and the veins of the spleen, mesentery, kidney, and bladder.

Distoma ringeri, or **bronchial fluke,** is the cause of the parasitic hemoptysis endemic in China and Japan. The para-

site is ovoid, eight mm. to ten mm. long, three mm. to six mm. wide.

Ascarides, or Round Worms.—The *Ascaris lumbricoides* is a yellowish or yellowish brown worm varying in length; female, 15 cm. to 30 cm.; male, 9 cm. to 20 cm., striated transversely with four longi-

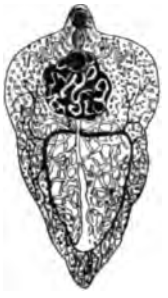


FIG. 205.—DISTOMA HEPATICUM.

FIG. 206.—BILHARZIA HÆMATOBIA, MALE AND FEMALE, THE LATTER IN THE CANALIS GYNÆCOPHORUS OF THE FORMER. —(*After Leuckart.—Gould.*)

FIG. 207.—ASCARIS LUMBRICOIDES AND EGGS.—(*Coplin and Bevan.*)

tudinal bands. They are most common in children, occupying the upper portion of the small intestine, from which they may wander into the bile-ducts, stomach, œsophagus, nose, Eustachian tube, and larynx. The number in any case varies;

rarely are they present in large numbers. The ova are elipsoid, 0.06 mm. in their longest diameter, with a dense enveloping membrane.

Oxyuris vermicularis, *thread-worm* or *pin-worm,* inhabits the colon and rectum, occasionally in the female invading the vulva and vagina. The female parasite is from 8 mm. to 12 mm., and the male three mm. to six mm., in length.

Trichina Spiralis.—Infection by this parasite occurs by ingesting trichinous flesh. In the muscle the parasite, in the

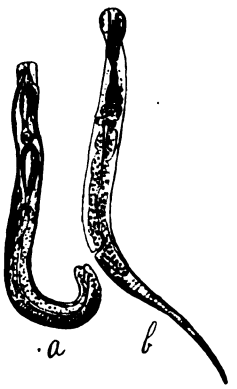


FIG. 208.—OXYURIS VERMICULARIS.—(*Coplin and Bevan.*)
a. Female. *b.* Male.

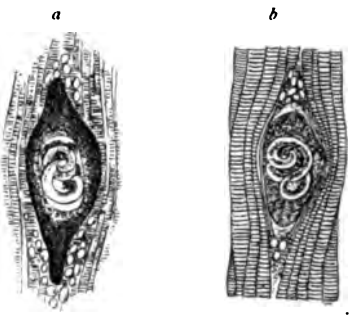


FIG. 209.—TRICHINA SPIRALIS.—(*After Leuckart.*)
a. Encapsulated. *b.* Same with calcific capsule.

form of its embryo, will be seen as a coiled-up worm 0.05 mm. in length, surrounded by a capsule which at first is translucent, later becoming opaque, and eventually calcareous. If meat containing the embryo be eaten, the capsule is digested in the stomach, the embryo liberated, and its final development into the adult worm completed in the small intestine. The fully-developed female trichina measures three mm. to five mm., the male about half as much. The embryos hatched in the intestine wander into the mucosa, penetrate the wall of the

intestine, and become widely disseminated throughout the organism. The destination of the worm seems to be in the muscles; here it coils up, and is surrounded by a capsule partly produced by the reaction of the surrounding tissue. The changes which this capsule undergoes have already been noted. *Trichiniasis* is the term applied to the symptoms and lesions observed at the time of dissemination of the embryo.

Anchylostoma duodenale, Strongylus, or **Dochmius duodenalis** is associated with certain forms of anemia and Egyptian chlorosis. The male is about eight mm. in length, with a distinct bursal enlargement at the tail end. The female is much the larger, measuring, not uncommonly, 15 mm. By a series of tooth-like hooks with which the mouth is provided, the parasite attaches itself to the mucous membrane of the duodenum. Inflammation of the intestinal mucosa results, and, in some cases, this may assume a hemorrhagic form; profound anemia is one of the most constant associated phenomena. Infection occurs by drinking poluted water. In Egypt, Italy, Russia, and South American States the inhabitants not uncommonly suffer, but in North America but little is known of the parasite. The recognition of the condition during life is often effected by finding the ova in the stools. The ova are about 0.05 mm. in diameter, egg-shape, with a thin enveloping membrane.

FIG. 210.—CEPHALIC EXTREMITY OF DOCHMIUS DUODENALIS, PROFILE AND FRONT VIEW.—(*After Leuckart.—Gould.*)

Filaria.—In the lower animals filaria are not uncommon, but in the blood in man few of them have been identified with disease. The **Filaria sanguinis hominis,** so constantly associated with chyluria, hematochyluria, lymph-scrotum, and a condition resembling elephantiasis, is probably the most im-

portant. The male is small, and rarely found. The female is a thread-like worm four cm. to seven cm. in length and 0.25 cm. in diameter ; the head is club-like ; about one mm. behind the head is the opening of the vagina, which terminates in a bifid uterus, extending backward almost the entire length of the parasite, and crowded with embryos in all stages of development. An alimentary canal runs the entire length of the parasite.

The worm inhabits the lymphatics, into which it pours an enormous number of embryos. These are near 0.25 mm. in length, 7 μ in thickness, about the diameter of a red blood-cell, thus permitting their transfer from point to point in the circulation, to which they gain ingress through the lymphatics. Their presence in the peripheral blood is peculiar, in that it is cyclic, appearing only in the night or sleeping-hours. In most cases they can not be found in the day, but in individuals who sleep during the day the parasites can then be found. If, at the appropriate time, a drop of blood be drawn and examined in the fresh condition, but little difficulty will be found in detecting the parasite in embryo ; the movements are rapid, and the enveloping membrane or shell is delicate, transparent, and so elastic that it in no wise impedes the movements of the embryo.

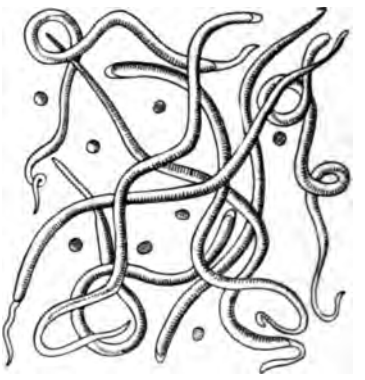


FIG. 211.—EMBRYOS OF THE FILARIA SANGUINIS HOMINIS. FOR COMPARISON OF SIZE A FEW BLOOD-CELLS ARE ALSO SHOWN.—(*From Leuckart, after Lewis.—Gould.*)

The presence of the parasite is not suspected until blocking of some of the lymph-channels gives rise to one of the conditions above mentioned. The parasite is abundantly present in the inhabitants of the tropics and subtropics.

The **Filaria medinensis,** or Guinea-worm, of which only the female is known, is about 60 cm. to 90 cm. in length and two mm. in diameter and usually solitary, although not always so. The parasite enters with the food, probably both male and female, but only the latter develops. It penetrates the mucosa and eventually reaches the subcutaneous tissues, in which it completes its development. During the latter period it may be palpable under the skin ; finally suppuration ensues and the worm is cast off, with innumerable ova, which enter water, where, in the cyclops, further development occurs. The parasite has been observed in a patient, a native, and always a resident, of Philadelphia, but it is rare in this country.

Among the other filaria occasionally observed in man are : *Filaria bronchialis,* found in the bronchi ; *Filaria loa* (three cm.), found in the conjunctiva ; *Filaria hominis oris,* in the mouth ; etc.

Trichocephalus dispar, or whip-worm, inhabits the large intestine ; the female measures about five cm., the male is shorter. The anterior two-thirds of the body is thread-like, the remainder conic, and in the male rolled like a spring.

Tapeworms, or Cestodes.—Of these, four only are of sufficient interest to merit description.

(*a*) **Tænia mediocanellata** or **saginata,** or **beef tapeworm.** The head is quadrate, 1.5 mm. to 2.25 mm., surmounted with four suckers arranged in a quadrangular outline, in the center of which is a fifth rudimentary sucker ; the head is void of hooklets, and hence the worm is spoken of as the "unarmed tapeworm." The head is attached to a slender neck, varying in length and terminating in the first link, proglottis, or segment, terms used synonymously. The segments when fully developed are between eight mm. and ten mm. broad and about 18 mm. long, and thicker than the proglottides of the Tænia solium ; like all tapeworms, each segment is hermaphroditic. The genital pores are placed

laterally; the uterus shows dichotomous branching more characteristically than the Tænia solium; the number of branches varies, but is approximately about 15; the segments are commonly thrown off spontaneously, while the Tænia solium rarely sheds a single proglottis. The length of the worm varies greatly; the number of segments may exceed 1000 and the entire worm measure between four meters and ten meters. The ova constantly appear in the stools, and the segments show the uterus distended with them.

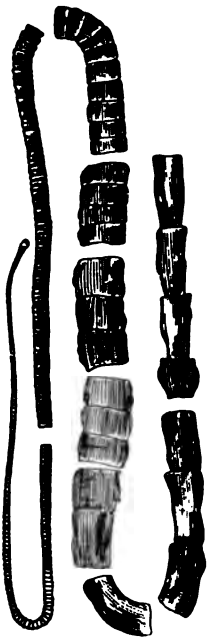


FIG. 212.—TÆNIA SAGINATA.—(*Gould.*)

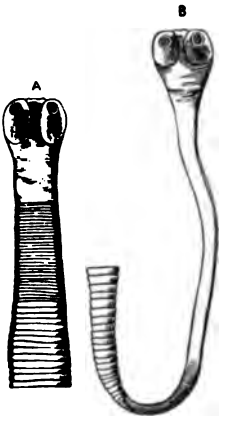


FIG. 213.—CEPHALIC END OF TÆNIA SAGINATA.
A. Retracted Head. B. Extended Head.

Each ovum is 0.03 mm. in its long axis, is ovoid or egg-shaped, with a striated outer membrane and a thick shell. The eggs and segments thrown off in the feces are ingested by the ox; the larva or juvenile parasite is liberated, and reaches the muscles, for the most part, although they have been observed in the heart, lungs, and liver. Here develops a cyst varying in size

from two mm. to one cm. in diameter, whitish in color, and in outline oval. In this is the larval worm; the cyst wall is of connective tissue. In this stage the parasite is known as Cysticercus saginata. Beef rarely contains many, and their small size not uncommonly causes cysts to be overlooked. Beef containing the cysts is said to show "measles." It is not known that man suffers from Cysticercus saginata.

(*b*) **Tænia solium,** also known as the **pork tapeworm, solitary tapeworm,** and **armed tapeworm.** The name Tænia solium, or solitary tapeworm, is not appropriate, as the

FIG. 214.—HEAD OF TÆNIA SOLIUM. ON THE RIGHT, EGG OF TÆNIA SOLIUM.—(*Gould.*)

FIG. 215.—CYSTICERCUS CELLULOSÆ. COMPLETION OF HEAD FORMATION.—(*After Leuckart.—Coplin and Bevan.*) × 12 diameters.

pork tapeworm is more commonly multiple than the beef tapeworm; indeed, Leidy regarded the latter as rarely multiple. The adult parasite is a soft, white, band-like worm, rarely over four meters in length. The head is round, 0.5 mm. to one mm. in diameter; there are four discoid or cup-like suckers and a centrally placed papilla, proboscis, snout, or rostellum, surmounted by two rows of hooklets, each row having 12 to 14 hooklets; the hooklets of the inner row are the larger. The neck is very thin, about 2.5 cm. in length, terminating in the gradually-developing segment. The segments are ten

mm. to 12 mm. long and six to eight mm. broad. The segments differ in this respect from the beef tapeworm; the segments nearer the head may be much broader than long. The uterus is broader, coarser, and the median tube larger, with fewer branches—six to ten, but little over half the number commonly seen in the beef tapeworm. The eggs are about the same size as those of the beef tapeworm, 0.03 mm., but more spheroid.

The **scolex, larval, juvenile,** or **cysticercus form** of the Tænia solium has long been known, but Küchenmeister, by feeding experiments, demonstrated that the so-called **Cysticercus cellulosæ** was but the larval form of the Tænia solium. The larva are most frequently developed in the hog, gaining ingress as already described when considering the similar stage in the beef tapeworm. The habits of the hog, however, render measles much more common in that animal than in the ox. Either by the accidental contamination of the hands and subsequent ingestion of the ova, or possibly by regurgitation during vomiting, occasionally the ova reach the human stomach; as in the beef larvæ in the ox, the liberated larva of the solium in man may become widely disseminated. When it lodges a cyst follows, and whether in man or the hog a "measle" results. The cyst formed is much larger, as a rule, than in the ox, and may attain the size of 20 mm., the beef measle rarely exceeding seven mm. While the beef measle is unknown in man, this form is not infrequent. The method of invasion is probably the same from both cysticerci; both the embryos, when liberated in the stomach, have six hooklets, arranged in pairs, by which they tear and propel their passage through the wall of the stomach or intestine.

(*c*) **Tænia lata, broad tapeworm,** or, more correctly named, as it belongs to another genus, **Bothriocephalus latus.** The head is clavate, rather elongated, has a long elliptic sucker

on each side, measures about 1.5 mm. long by one mm. wide, and is without either rostellum or hooklets. The fully-developed joints are from two to four times as broad as long; the breadth of the link may reach 1.8 cm. The genital aperture is always on the one side, the ventral aspect, and is

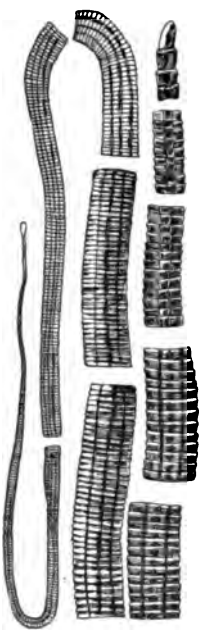


FIG. 216.—BOTHRIOCEPHALUS LATUS.—(*After Leuckart.—Gould.*)

FIG. 217.—FREE-SWIMMING EMBRYO OF THE BOTHRIOCEPHALUS LATUS.—(*After Leuckart.—Gould.*)

FIG. 218.—CLUB-SHAPED HEAD OF THE BOTHRIOCEPHALUS LATUS.—(*After Leuckart.—Gould.*)

A. Seen from the edge. B. Seen from flat surface.

central. The eggs are brownish, oval, 0.07 mm. in length, and the shell furnished with a lid or operculum, through which the embryo escapes after some months in water. Braun has observed in pike and trout scolices, believed to be of the bothriocephalus, and by feeding the fish to dogs has

led to the development of the tapeworm in the dog. The fully-developed worm is said to be the longest of tapeworms.

(*d*) **Tænia flavopunctata** is a short tapeworm, not exceeding 40 cm. in length. The segments vary in length from 0.2 mm. at the neck to 0.5 mm. when fully developed, and in breadth from 0.6 mm. to 2.5 mm. at the same points. A peculiarity of the segments is the alternation of fertile with sterile segments, the former so laden with eggs as to obscure its interior and being much larger than the non-ova-bearing links. The eggs are spheroid, brownish in color, with a diameter of 0.07 mm. Nothing is known of the larval stage of the parasite.

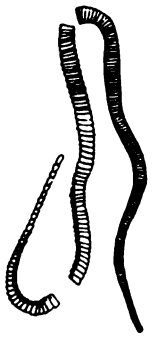


FIG. 219.—TÆNIA FLAVOPUNCTATA.

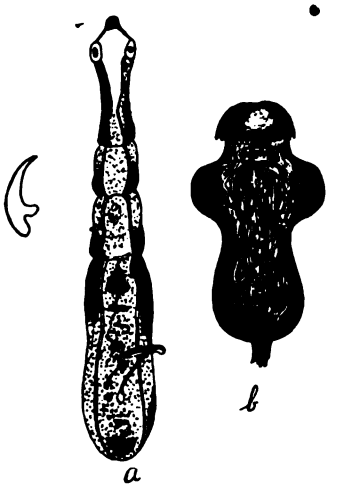


FIG. 220.—TÆNIA ECHINOCOCCUS.—(*After Leuckart.—Coplin and Bevan.*)

a. Adult parasite. *b*. Head of Echinococcus veterinorum. On the left a detached hooklet, as seen in fluid from cyst.

Tænia Echinococcus, or Dog Tapeworm.—The sexually mature worm inhabits the intestine of the dog and wolf. It is an insignificant parasite in appearance when compared with the larger forms, rarely attaining a length of five mm. When fully developed there are four segments; the anterior is

slender and is continuous with the head, the following segment is the shortest and the last the longest; often more than half of the length of the parasite is in the last segment; from time to time the large link is thrown off, so that it is not uncommon to find but the three proglottides. The parasite is short lived, and probably the least prolific of the tapeworms; this is compensated for by the proliferative power of the parasite in the juvenile or larval stage. The anterior segment, or scolex, is surmounted by four suctorial discs, anterior to which, between the quadrately placed sucking discs, is the rostellum, with its hooklets, numbering 30 to 40. The adult parasite is not found in man. The ova thrown off by the parasite, entering the alimentary canal of man and some lower animals, hatch the embryo, which, wandering into the tissues of an organ, develops into a cyst—the encysted parasite. These cysts occur in three forms:

(1) **Echinococcus scoliciparíens, Echinococcus granulosus,** or **Echinococcus veterinorum,** is a bladder-like cyst, varying in size, often five cm. to 15 cm., or even 20 cm., in diameter. The wall of the cyst is formed of two layers, as a rule, easily distinguished from adjacent structures and from each other. The outer layer is supplied by the invaded organ, and is called the cuticular membrane, the tissue of which shows distinct lamination; the inner layer, which is finely granular, constitutes the granular or parenchyma layer. When the cyst has attained a diameter of two cm. to ten cm., the development of brood capsules begins. These will be found attached to the granular layer, first as dot-like bodies, later as distinct cysts in which many young parasites occur; hence they are spoken of as brood cysts. The heads or scolices projecting into the cyst are about 0.3 mm. long, have developed four suckers, and a rostellum with attached hooklets; the interior shows a vascular system and sometimes granular, chalk-like bodies within; at times a parasite may be

found with the scolex invaginated into the posterior part of the body as though retracted.

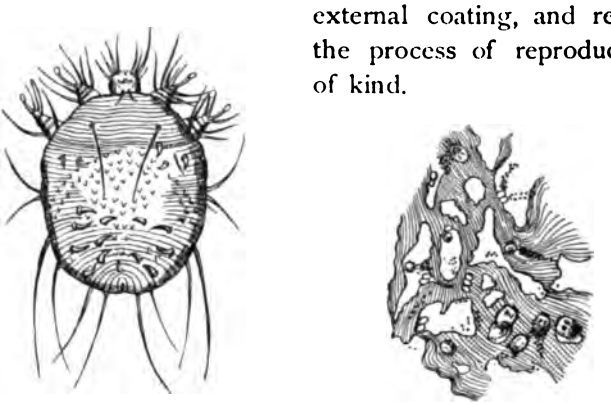
(2) **Echinococcus hydatidosus, Echinococcus altricipariens,** or **Echinococcus hominis,** is characterized by the development of daughter-cysts, probably from degeneration of the brood capsules already described. From the daughter-cysts another generation of parasites may develop, forming still another series of cysts. The number of daughter-cysts may be enormous; as given by Thoma, 1000.

(3) **Echinococcus multilocularis** is unlike the other forms of echinococci, the cysts never attaining any great size, but occurring in enormous numbers. The liver is the common site of this form, which is very rare in the other organs. Earlier observers regarded the growth as an alveolar, colloid tumor. The cysts rarely attain a diameter of over one cm., are spheric or ovoid, the wall formed by a dense connective-tissue membrane, which, under the microscope, may contain still smaller alveoli; the alveoli are filled with a more or less gelatinoid or colloid material containing a few of the histologic elements of the scolex. Often only on prolonged examination can these be demonstrated. The cysts may communicate with one another.

Site.—Echinococci may occur almost anywhere, but over 45 per cent. of the cysts are found in the liver. (See "Cysts," p. 215.)

Acarus scabiei (arachnida), the parasite which causes scabies or itch, is known as the **itch-mite** or **Sarcoptes hominis.** The female is nearly double the size of the male, and can often be picked out of the furrows found in the skin in cases of itch. The parasite is two mm. to five mm. in length, and over one-half as broad. It possesses four pairs of legs, two pairs anteriorly and two posteriorly. From each of the foremost pair of the anterior legs extend delicate processes, supplied at the distal end with discoid terminations for

attaching themselves to surfaces; in the male these addenda are on the hindermost pair. The other legs end in a bristle. The posterior border has a number of bristle-like hairs; similar hairs are seen on the rounded head of the mite. The parasite burrows into the epidermis, in which it forms cavernous systems attended with inflammation of the adjacent mucous layer. In the cuticular caverns the female deposits her eggs, which hatch into young mites. These burrow, shed their external coating, and repeat the process of reproduction of kind.



A B

FIG. 221.

A. Acarus scabiei. B. Portion of epidermis, showing the burrows with their contained eggs.—(*After Leuckart.—Gould.*)

Leptus autumnalis, or **harvest-mite** (larva of Trombidæ), is a red-colored parasite deposited upon the skin from grass, bushes, and certain cereals; it induces inflammation by its bite or by boring into the epidermis.

Pentastoma denticulatum is the juvenile form of the Pentastoma tænioides. The mature female is 50 mm. to 125 mm. in length, and six mm. to ten mm. broad; the male is much smaller, 15 mm. to 25 mm. long, and two mm. to five mm. in breadth. The larva is between three mm. and five mm. in length, and one mm. to two mm. wide,—an egg-shaped mass occasionally found in the viscera. The mature worm is found in the

frontal, nasal, and maxillary sinuses of some of the domestic animals.

The demodex, or **Acarus folliculorum hominis,** inhabits the ducts of sebaceous glands and occasionally the hair follicles. It is broad just back of the head, from which point it tapers down to a blunt hinder extremity; at the broadest part are four short, thick legs. The length of the parasite varies greatly between 0.5 mm. and one mm., and is usually about one-tenth as broad at the widest point.

Ixodes ricinus, or *wood-tick,* inhabits wood which is decaying in dry places (dry rot of timber), from which it may get on dogs, and occasionally on man. The head is black or brownish, and supplied with a boring disc, which penetrates the skin, and through which the parasite sucks blood.

Pediculus capitis, Pediculus ordinarius, *head-louse,* or *common louse,* inhabits the hairy scalp. The adult parasite is about two mm. to three mm. in length, and, pathologically, is an epizoon, securing nourishment by attacks upon the skin. The irritation produced by the bites is sometimes followed by inflammation, which may be eczematous in character. The eggs are oval, with slightly flattened ends, attached to the hair by a chitinous cement, which also covers them. An egg hatches out in from seven to ten days.

FIG. 222.—PEDICULUS PUBIS.

Pediculus vestimenti, Pediculus corporis humanus, *clothing-* or *body-louse,* inhabits the clothing, in which it deposits its eggs. The fully-developed parasite is considerably larger than the head-louse. From the clothing the parasite makes incursions to the skin, from which it obtains nourishment. The bites induce changes similar to those of the head-louse.

Pediculus pubis, Pediculus inguinalis, Phthirius pubis

or **inguinalis**, or *crab-louse*, infests the hairy pubis, axilla, and, rarely, the beard and eyebrows. The parasite is smaller than either of the above. Its habits are practically the same as the head-louse.

Cimex lectularia, Cimex hirundinis, or *bed-bug*, dwells in beds, floors, and cracks of wood-work, from which it invades the skin, the bites producing slight inflammatory lesions. The adult parasite is three mm. to six mm. in length; the eggs are laid between the months of April and October, and require eleven weeks to hatch and develop the mature parasite.

Pulex irritans, Pulex hominis, or *human flea;* the **Pulex serraticeps, Pulex felis, Pulex canis,** or *dog-flea.* The two parasites closely resemble each other, and by some are held to be identical. They infest the hair of the dog and cat, from these animals wandering to man. Closely related to these is the *sand-flea*, **Pulex minimus cutem penetrans,** or **Pulex penetrans,** an excessively annoying parasite, smaller than any of the above, and found in the sandy areas of the tropics and subtropics.

The **mosquito** and certain forms of the *gnat* belong to a subdivision of the parasitic genera known as the *culex.* The *Culex ciliatus*, or *large mosquito;* the *Culex equinus*, or *horse mosquito;* the *Culex damnosus*, or *common mosquito* of the lowlands of the Eastern States, and the *Culex pipiens* of Europe, are the most important members of the culex group. The local lesions induced by these parasites, while not wholly unimportant, are now considered of more importance than formerly. It is held by Manson and others that these parasites are intermediate hosts for the smaller parasites, the larva of the filaria, and that they inoculate the human organism with the parasite of malaria.

Maggots, occasionally seen in dead tissues, and, before the antiseptic methods of to-day, one of the parasites found in wounds, are the larval form of certain flies. The eggs deposited

on the wound surface, dressings, etc., hatched, the resulting juvenile parasite being known as a *maggot.*

Hematozoon, or **Hematomonas malariæ,** also known as the **Plasmodium malariæ.** During the period in which the temperature of the malarial patient is rising and approaching the chill stage, and in many cases quite independent of the paroxysm, if a drop of blood be prepared for examination as directed (see "Technic of Blood Examination," p. 78), the parasite will commonly be readily found. Presuming that the examination be begun at the period when the chill is in progress, or impending, in the tertian intermittent form of malaria: The parasite is now in the sporulation stage, a period in the cycle of its development when not of easy demonstration. A magnification of about 1000 diameters ($\frac{1}{12}$ of an inch oil-immersion) will be found convenient, but not absolutely necessary, as the discoverer of the parasite, Laveran, commended a magnification of 600 diameters ($\frac{1}{6}$ or $\frac{1}{8}$ of an inch objective, with a good eye-piece). Carefully focusing on a part of the field where the red blood-cells are thinly spread, the slide is slowly moved, a close watch being kept for pale bodies in the corpuscles, or pale corpuscles, in which the parasite is to be looked for. At times a red cell will be found, with a mulberry-like mass occupying the most of the cell; the cell is likely to be deformed, ovoid in outline, with loss of evident biconcavity. (See Fig. 223, A_1, A_2, A_3, A_4.) A little later the red blood-cell breaks up and the **sporulating plasmodium** is freed in the blood. Its recognition in this stage is most difficult, the somewhat irregular hyaline bodies not readily recognizable until they again attach themselves to a red blood-cell. Shortly after the paroxysm red blood-cells appear with the so-called **epicorpuscular forms,** the hyaline ameboid bodies usually eccentrically placed, almost never round, but irregular, with out-branching, pseudopod-like arms, and, if the slide is warm or the observation made in a warm room, the hyaline

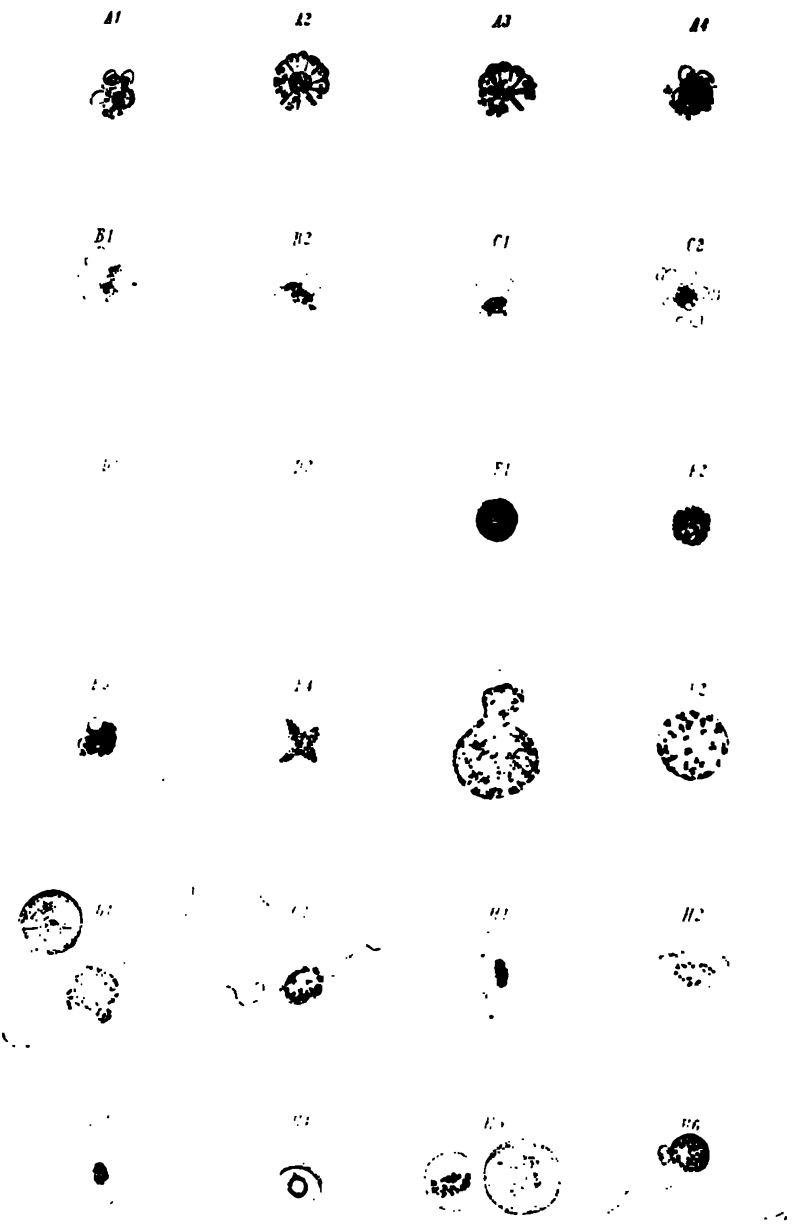


FIG. 223.—ILLUSTRATING DIFFERENT FORMS OF THE MALARIAL ORGANISMS WITH THEIR STAGES OF DEVELOPMENT.—(*Tyson's "Practice of Medicine."*)

A_1, A_2, A_3, A_4. Sporulation stage. B_1, B_2. Sporules separating. A_1, A_2, A_3, A_4, B_1, and B_2. Stages in the so-called rosette form of the parasite. C_1, C_2. Free sporules. D_1, D_2. Epicorpuscular forms. Non-pigmented ameboid bodies. E_1, E_2, E_3, E_4. Intracorpuscular forms, with varying amounts of pigment. F_1, F_2. The large extracorpuscular body. G_1, G_2. The flagellate forms. H_1, H_2, H_3, H_4, H_5, H_6. The crescent-shape parasite.

body changes its shape and position. It is upon the ameba-like motion that we can most readily assert its presence. The so-called vacuoles or hydropic spots which are occasionally seen in the blood may mislead the inexperienced and unwary ; the knowledge of their possible presence should prevent such a possibility. As soon as the parasite becomes fully **intracorpuscular** and advances in its growth, there appears agmination of the red blood-cell coloring-matter apparently into the parasite, which, therewith, assumes the **pigment stage ;** now it is most easily recognized ; it occupies a variable extent of the blood-cell, and has within it the moving granules of pigment ; if the cell be cooled, or in the least dried, pigment motion ceases, and the quiet pigment closely resembles extraneous material which microscopists roughly designate as dirt. The freshly-drawn blood with the moving pigment within the parasite, and the latter again within the red cell, offer no excuse for failure in identification. (See Figs. 81 and 82, p. 84, partly diagrammatic representations of the non-pigmented and pigmented parasites.) The number of parasites in any specimen of blood varies, but in a fairly-marked case one should expect at least one to every two or three fields, but a more extended search may be necessary.

As the development of the parasite progresses, faint lines radiate from the center toward the periphery near which each pair of marginal markings are joined by a short arc ; near the outer extremity of each of these wedge-shaped masses we see a small granular body, presumably the nucleus. The clumps of these wedge-shaped masses around a common center give the parasite a **rosette** shape. This rosette may or may not be surrounded by a visible rim of the remaining red corpuscle. This is the mulberry-like form which is the sporulating stage, ready to free the spores, at which time the malarial paroxysm usually occurs. The freed sporules are not recognizable in the peripheral blood, but probably are liberated in the large

viscera, in which they attach themselves to the red corpuscles and again appear in the peripheral circulation.

The differentiation between the tertian and quartan parasites is based upon certain differences in the morphology at various stages in their development.

	Tertian Parasite.	Quartan Parasite.
Size.	About that of red blood-cell.	Smaller.
Pigment.	Fine, light, active.	Coarse, dark, less active than tertian.
Red Blood-corpuscle.	Swells and fades in color.	Shrinks around the parasite and deepens in color.
Sporulation Segments.	Fifteen to twenty or more.	Usually not over six, at times fewer.
Cycle.	Completed every other day.	Completed every third day.

The parasite of irregular malarial fever, the *estivo-autumnal type*, is less regular, so far as we can ascertain, in the cycle of its development, but presents certain characteristics by which its identification is assured. In the earlier stages it may escape notice, as it is not abundant in the peripheral circulation. The small *hyaline bodies* are few, very small, with scant pigmentation, and the red cells much shrunken, the hemoglobin, with but little granulation, surrounding the parasite, leaving the outlying segment of the red blood-cell but faintly, if at all, colored. The later stage of the cycle occurs in the viscera. Later there appears the **crescentic form** upon the recognition of which the diagnosis so largely depends. Crescents are not seen until the fever persists several days. They are assumed to develop from the hyaline form, which gradually enlarges, loses its motility, and becomes crescentic, with agmination of its pigment granules near its center. Crescents occur in freshly-drawn blood, and, when observed under suitable conditions,

may be seen to assume elliptic, ovoid, and round forms ; when the round form is attained, the pigment granules become actively motile, which may be a step toward sporulation.

Extracorpuscular and **flagellate forms** of the malarial parasite are seen as changes not presumed to occur in the circulating peripheral blood. The former are presumed to be the same as the intracorpuscular bodies liberated from the blood-cell by postmortem changes, and not observed until some moments after the blood is drawn. At times, particularly if the blood drawn be kept in a moist chamber and warmed to near the normal blood heat, there appears a series of phenomena, by attentive attention to which, flagella may be demonstrated. First around, or near, a malarial parasite may be seen a group of red corpuscles in active motion as though being lashed about ; by careful focusing we may make out a filmy, almost imperceptible, whip-like process, attached to the malarial parasite and in active motion ; it may show a few pigment granules along its length, and possibly at its end a slight bulbous enlargement in which there may be pigment. Occasionally a flagellum may become detached and show active motility, progressing among the corpuscles through several fields.

The above brief description applies to the fresh slide of blood. When, for any reason, staining is found necessary, the use of Plehn's method will stain the parasite, the methylene-blue taking in the nucleus and faintly the protoplasm of the parasite, while the eosin colors the red blood-cell. (See section on " Technic of Blood Examination," p. 82.) The methylene-blue staining of the leukocytes must not be forgotten by the novice, and the possible overlying of red cells on improperly fixed or shrunken leukocytes must not be misjudged.

QUESTIONS.

(1) What are psorosperms? (2) Describe the Cercomonas intestinalis. (3) To what group of animal parasites do the amebæ belong? (4) Describe the Amœba coli. (5) Name some of the flukes associated with disease. (6) Describe the Ascaris lumbricoides. (7) Describe the Oxyuris vermicularis. (8) Describe the Trichina spiralis. (9) Describe the Anchylostoma duodenale. (10) Describe the Filaria sanguinis hominis, adult and embryo, and which is found in the blood? (11) What other filaria are occasionally found in man? (12) Describe the Trichocephalus dispar. (13) Describe Tænia mediocanellata. (14) In what animal does the larval parasite develop? (15) What is "measles" in beef? (16) Describe the Tænia solium. (17) What is pork measles? (18) Describe the Bothriocephalus latus? (19) Describe the Tænia flavopunctata. (20) Describe the Tænia echinococcus. (21) Name forms of echinococcus cyst. (22) In what organs are these cysts most frequent? (23) Describe the Acarus scabiei. (24) What lesions may it produce? (25) Describe the Pentastoma denticulatum. (26) Describe the Acarus folliculorum hominis. (27) Of what parasite are the mosquito and gnat presumed to be intermediate hosts? (28) What are maggots? (29) Describe the plasmodium of malaria. (30) How examine for the parasite? (31) At what time is it best to search for the organism in the peripheral blood? (32) What magnification is best for their demonstration? (33) Describe the epicorpuscular bodies. (34) Describe the pigmented bodies. (35) In what stage of their cyclic life do rosette forms occur? (36) What seems to determine the occurrence of the malarial paroxysm? (37) How differentiate between the tertian and quartan parasites? (38) Describe the organism of estivo-autumnal malaria. (39) Under what conditions do the extracorpuscular and flagellate forms occur? (40) Describe these. (41) What are the color reactions of the parasite to Plehn's stain?

CHAPTER X.

TEMPERATURE CHANGES.

INTOXICATIONS—INFECTIONS.

The temperature of the human body remains practically constant, or about, at 37° C. There are normally for each individual certain variations above or below the mean for the twenty-four hours; the maximum fall, in health, rarely exceeds 0.5° C., and is, for most persons, always at about the same hour of the day; the same is true of the daily rise, so that, between the daily maximum and minimum, there is commonly about 1° C. of fluctuation. This daily curve of the temperature follows about the same course each day, so that the maximum is reached between 4 and 6 P. M., and the minimum between the same hours A. M.; this cycle for any given individual is nearly uniform, but no two persons are likely to have identical rhythmic curves. The following table, from Thoma, compiled by Jürgensen and Liebermeister, indicates the temperatures of different hours in the day:

Time of Observation.	Temperature in the Rectum. (*Jürgensen*)		Temperature in the Axilla. (*Liebermeister.*)	
	F.	*C.*	*F.*	*C.*
In the morning in bed,	(98°)	36.6°	(97.8°)	36.5°
Before breakfast,	(98.18°)	36.7°	(98°)	36.6°
After breakfast,	(98.36°)	36.8°	(98.7°)	37.0°
In the forenoon,	(98.8 °)	37.1°	(99.18°)	37.3°
Before lunch,	(99.18°)	37.3°	(99°)	37.2°
After lunch,	(99.36°)	37.4°	(99.18°)	37.3°
In the afternoon,	(99.5°)	37.5°	(99.36°)	37.4°
Before dinner,	(99.7°)	37.6°	(99°)	37.2°
After dinner,	(99.36°)	37.4°	(98.8°)	37.1°
Before going to bed,	(98.8°)	37.1°	(98.36°)	36.8°
During the night,	(98.7°)	37.0°	(98°)	36.6°
	(98.36°)	36.8°	(97.18°)	36.2°
	(98.36°)	36.8°	(97.18°)	36.2°

The hypotheses and theories presumed to explain the mechanism of temperature regulation are based upon certain well-established facts. Heat, representing the cellular or tissue activity, is generated within the body by the oxidation of food supplied or stored, or of the tissues themselves, distributed largely by the blood and lost chiefly from the skin and respiratory mucous membrane. The regulation of the body temperature must be through means addressed to one of three agencies: heat production, distribution, or dissipation.

Heat production occurs in every organ and tissue, but the greatest thermogenic activity is manifested in the muscles, including the heart, and in the large glandular viscera,—for example, the liver. The greatest heat production occurs in the voluntary muscles, including those of respiration. The heart muscle is presumed to afford a considerable supply of heat in the same manner as the other muscles, and in addition transmits force which is indirectly converted into heat by the friction of blood against the cardiac walls and also the walls of the arteries and capillaries through the resistance of which the blood-pressure is largely maintained. That the blood rises in temperature after passing through the liver is not a source of surprise, when we take into consideration the remarkable glandular activity of the organ.

The distribution of the blood is largely controlled by the nerves supplied to the arterioles, and, as the dissipation of heat is largely dependent upon the distribution of the blood, the influence of vascular innervation upon heat loss is one of the most important elements to be estimated. Exactly what determines the action of the vasomotor nerves, in the regulation of temperature, is one of the unsolved problems in normal and morbid physiology. It would appear that there is somewhere a center, possibly more than one, which presides over the body temperature by regulating at least heat dissipation, if not its production, but probably both. The theory

of heat regulation by the nerves implies a heat-regulating center, **thermotactic center,** with nerves controlling heat production, **thermogenic nerves**, nerves controlling heat dissipation, or **thermolytic nerves,** and, possibly, nerves which influence heat-producing tissues in a way antagonistic to the thermogenic nerves, **thermo-inhibitory nerves.** This complicated system is assumed to have its center in the medulla; this center, acted upon by certain agents, manifests disturbance through the fibers of some of the nerves indicated. In addition to one or possibly more centers in the brain or medulla, there may be in the cord or even larger ganglia subsidiary centers influencing a region, or regions, only. The production of heat by the oxidation of food and tissue elements, the distribution of the heat generated, and its final dissipation, are complicated phenomena which, with our existing knowledge, can be but imperfectly contemplated.

Subnormal Temperature.—A temperature below the mean normal of the active period of life occurs in some forms of anemia, follows shock and severe hemorrhage, is present in some forms of exhaustion or adynamia, and frequently follows marked elevations of temperature, particularly if prolonged; thus, after typhoid fever and pneumonia a period of subnormal temperature is often seen. The explanation of this condition lies probably in lessened heat production, although instances occur—as in the occasional cases of great cutaneous activity after hemorrhage and shock—in which more heat may be lost than normal; such a source for subnormal temperature, however, is rare. The reduction of temperature may also be caused by the circulation of certain poisons in the blood, as in diabetes, in which the temperature may sink 5° C. or even more. In this condition both heat production (thermogenesis) and heat dissipation (thermolysis) are probably at fault, the control and equalization of the two by the thermo-

tactic power having been perverted by the influence of the noxious agent circulating in the blood.

Pyrexia.—Under certain conditions there arises a chain of phenomena which the clinician recognizes as *fever*. There is disturbance of a number of functions; appetite, secretion and excretion, the circulation, respiration, and, in many cases, the central nervous system, show marked disturbances. With one or more of these phenomena there occurs the one constant element of fever, *elevation of temperature—pyrexia*. In moderate cases the temperature reached may not exceed 39° C.; in more severe cases it may reach 41° C., and in grave cases go beyond 42° C. Temperatures exceeding 55° C. have been observed.

Causes.—There can be no doubt that the most important causes acting in fever production are *bacteria and their products*. That the germs are not the essential element may be shown by the production of artificial temperature rises by the injection, into animals, of filtered and also sterile cultures of certain bacteria. The introduction of preformed poisons into the system gives rise to a chain of symptoms, the condition being termed an *intoxication*.

Microbic intoxications are not purely the outcome of laboratory experiment, but occur, with regretable frequency, in practice. The symptoms of some of the infections are purely the evidence of intoxications; in diphtheria the bacillus may be limited, even in fatal cases, to proliferation on the surface of the mucosa, many of the symptoms and all the lesions occurring elsewhere than at the point of growth, arising from the dissemination of the toxin through the lymphatics, and eventually its distribution by the blood. A simpler example of pure intoxication, one frequently cited, is the infection of a blood-clot in the uterus following labor. The bacteria generating the poison in the blood-clot may never gain ingress to

the living uterine tissues, much less to the circulation, but the products of microbic life pass by absorption into the blood, through which they directly or indirectly induce the phenomena of intoxication. A retained blood-clot between the flaps, in a recent amputation, becoming infected, acts in a similar manner. By reason of this danger, in addition to its mechanical interference with healing, surgeons recognize the necessity of avoiding "dead spaces" in which infection may be favored by lessening the protective influence of living tissues. The intoxication arising from the absorption of microbic products is known as **septic intoxication,** or **sapremia,** and the element absorbed—the bacterial product—is termed **pyrogenous.** A peculiar fact, often observed, is that in the brain the products of bacterial life may not induce fever. This may be explained in a number of ways; growing on different culture media bacteria produce alkaloids with different pyrogenous activity, and in the brain tissues the activity or character of the microbic toxin, by reason of some peculiarity in the pabulum supplied, may be changed; the very fact that the abscess involves brain tissue and that the same may be potential in controlling temperature or modifying it, may make the accident of location a determining factor in its influence on body temperature. Again, evidence is not wanting to show that dissemination of poisons is less rapid by absorption through brain tissue, and this may in part explain the absence of fever in some cerebral abscesses; it fails, however, to offer any reason for the subnormal temperature at times observed.

Intoxications arise, however, without the intervention of bacteria; in cocain, strychnin, and brucin poisoning, and following the introduction into the circulation of certain animal poisons, as from snake-bites, stings of scorpions, etc., typic intoxications occur. In not all of these is there elevation of temperature.

In addition to the toxic bodies introduced from without,

such as those just mentioned, and among which may be included mussel-poisoning, intoxications may arise from poison generated within the body—**auto-intoxications.** The latter includes **enterosepsis,** or **copremia,** an intoxication occurring from the retention of intestinal contents, as in chronic constipation. The toxic material here is not purely microbic, nor is it purely the result of retention and absorption of noxious agents purely of animal origin, but probably represents a mixture of the two causative factors.

There is another source of fever-producing, or pyrogenous material, in the tissue dissolution and the formation of certain exudates; the exudates thrown out in the process of repair, during the formation of blood-clots, as around fractured bones, and under similar conditions, contain some agent which, by absorption, produces elevation of temperature. The chemistry and even the identity of the body is still a matter for speculation. Brieger noted the constancy of fever and fibrin formation, and surmised that the cause of both was the ferment presumed to cause the separation of the liquor sanguinis into fibrin and serum; this view meets with general acceptation. The rise of temperature which follows a surgical operation, a fractured bone, or interstitial hemorrhage, is presumed to be due to this ferment, a pyrogenous material generated during the breaking up of certain tissues of the body, commonly blood. These fevers—**surgical aseptic fevers**—are not truly intoxications, as they do not arise from the introduction from without of preformed poisons, but their resemblance, in some points, to copremia permits of their mention with the intoxications, as illustrative of certain causes operative in the production of fever.

Local Infections.—In sapremia the poisons generated by the bacteria are elaborated outside of living tissues, and in septicemia the poisons are generated by the bacteria in the blood; intermediate between these are the local tissue infec-

tions, in which the bacteria invade living tissue, from which the microbic poisons are absorbed into the circulation, either directly, through the capillary walls, or indirectly, by the lymphatics. In diphtheria the bacteria may be residents on the surface of the mucosa only, the toxins disseminating beyond and inducing necrosis, more dead tissue, into which the bacteria grow; in some cases, however, the bacteria pass the dead membrane and infiltrate the living tissues; there is then a local infection of living tissues as well as a growth in the dead, or necrotic, overlying structures. Erysipelas, abscess formation, the initial lesion of anthrax, and, under similar conditions, many infections, are in part, primarily at least, but local infections, with dissemination or absorption of the microbic products giving rise to the phenomena of an intoxication, the blood escaping actual invasion by the bacteria. The local infections, with the systemic symptoms due to the absorption of toxins produced in the living tissues, stand intermediate between pure intoxications, such as sapremia and the mycoses of the blood.

Any infection, whether localized or widely diffused, may be **simple**, that is, *single*, or due to but one germ, as a pure or simple infection by the streptococcus of erysipelas. A simple or single infection may be followed by the introduction of a second germ; the additional infection is known as a **secondary infection.** As an example of the last-named infection, we have the infection of a tuberculous area with an organism of suppuration. A secondary infection may be followed by a **tertiary infection,** and so on. Again, we may have a number of infections occurring, so far as we can determine, at one time; the process is then said to be a **mixed infection.** It is interesting to note that in the mixed and secondary infections it is not necessary that all of the bacteria present should belong to the pathogenic class. If one of the microbes be disease producing and leads to tissue necrosis, the secondary

infection may be by a saprophyte living upon the dead tissue resulting from the necrotic processes induced by the pathogenic organism. As a rule, mixed and secondary infections are more grave than simple infections, because the additional ferments produced by the second germ can but intensify the dangers to which the patient is subjected. While of little practical importance, the fact remains demonstrated that certain bacteria are antagonistic to each other, and that two organisms can be selected in the laboratory, which, if introduced into an animal, will not prove fatal as quickly as one of them alone. This fact is not, in the present state of our knowledge, explicable, and can have little practical importance, as the conditions probably never occur except in experiment.

The fact that non-pathogenic bacteria live and produce noxious elements in the necrotic tissues produced by pathogenic bacteria, leads us to see how dead tissue, or tissue with its protective powers in a state of abeyance, as after extensive bruising or laceration, may permit the growth of bacteria which, in less injured tissues or healthy structures, would immediately succumb to the resistance of the animal. For these reasons injured structures and tissues, with greatly reduced nutrition, may need a protection from infection not demanded by healthy tissues.

Mycoses of the Blood.—In these we have the bacteria present and multiplying in the circulating blood, their products generated in the blood, and the intensity of the septic phenomena, augmented by the greater production of the poison, and, not having even the barrier of protection afforded by the necessity of osmosis or absorption, are enabled to engender lesions not presumed to occur—at least not to the same extent—in either sapremia or local infection. The term **septicemia** was meant to cover, probably, some local infections, as well as mycotic invasion of the blood, but particularly infection of the blood by the organisms of suppuration. That

the common pyogenic bacteria are not the exclusive source of septicemias is shown by the reported instances of clinically typic cases of the disease, without the presence of the pyogenic organisms, but associated with other bacteria, as the diplococcus of pneumonia in the case reported by Sangree. Not only do the organisms proliferate in the blood, but also, in occasional cases, we find them growing by implantation, *mural implantation*, on the walls of some part of the circulatory system, as the valves of the heart in ulcerative or malignant endocarditis. With this implantation on the walls of the blood-vessels, heart, sinuses, etc., we may have the development of thrombi, and from these emboli, or, possibly, in the blood massing of elements may lead to emboli, emboli formed in transit ; the last is a questionable hypothesis. The emboli formed in blood, containing bacteria, are, of course, septic, and engender at their point of lodgment the changes already considered when discussing embolism. The embolic production of abscess is the essential element of **pyemia,** a disease recognized by the surgeons as septicemia plus the infected emboli to which we point as explaining metastatic abscesses. (See Thrombosis and Embolism, pp. 141 and 148.)

The fever which accompanies the septic processes is peculiar in the remarkable exacerbations which usually occur daily, and, in the graver forms, by the addition of repeated **rigors or chills.** Rigors are not restricted to septic processes, but occur also after hemorrhage, occasionally after shock, and as a poorly understood purely nervous manifestation ; they constitute the most marked phenomenon of the malarial paroxysm.

During the cold, or chill, stage there is a determination of the blood to the large glandular viscera and venous trunks ; the skin is thus deprived of its normal heat by the deficiency of its blood supply, and the cooling of the cutaneous nerves affords the explanation for the patient's sense of intense chilliness. That

the low temperature is purely a cutaneous phenomenon is shown by the thermometer. If we take the temperature in such a way as to estimate the actual blood-heat,—as in the rectum, mouth, or axilla,—preventing heat dissipation at the point where the temperature is being taken, we find the temperature above the normal. The deficiency of the cutaneous circulation lessens heat dissipation, and probably at the same time heat production is increased. Certainly in some fevers there is an increase of heat production, as abundant evidence is not wanting to show that heat dissipation may be greater than normal, and elevation of temperature persist—a condition impossible without persistent overproduction. After persisting a varying length of time, the chill ends by a return of the blood to the skin and usually rapid heat dissipation, though by no means always, followed by a marked decline in body temperature.

Whether preceded by a chill or not, the acme of the temperature rise is commonly followed by a progressive decline, associated with hyperactivity of the emunctories, particularly the skin. This gradual decline usually begins in the afternoon or early evening and progresses through the night, with the early morning temperature the lowest, the rise beginning at this time and reaching its height during the afternoon. During the twenty-four hours fever may disappear, only to reappear in a few hours ; this type is said to be *intermittent ;* in the *remittent type* there is more or less marked remission, but no period of complete apyrexia.

The causes active in producing this rhythmic alteration in temperature are obscure. It is maintained that the accumulation of pyrogenous material and its tendency toward fever production in the system is at first compensated for by the thermotactic powers ; eventually, the failure to excrete the poison as rapidly as produced, permits of such excessive accumulation that the heat-regulating forces are inadequate to the task of maintaining a constant temperature. This is followed by a rise which con-

tinues until the exhausted centers, which normally responded to slight temperature variations by adjustment of the mechanism between heat production and heat dissipation, respond to the more urgent demand for heat dissipation by a pseudocrisis, during which the temperature falls. The depressed or exhausted center, not responding to the slight changes which would affect it in health, now permits another accumulation of heat, which again sets it off, the process being repeated day after day so long as the pyrogenous material is thrown into the circulation.

With the rise in temperature, certain circulatory phenomena manifest themselves. Thus, for every degree Fahrenheit (.55° C.) which the body temperature rises, the pulse-rate is increased ten beats; this observation is approximately correct for temperature rises within two or three degrees, but with higher temperatures a greater rise occurs; Liebermeister showed that for the 1° C. above 41° C., the number of heart beats increased 27.

During the earlier stages of fever the *blood-pressure* is likely, also, to rise, but the early relaxation of the vasomotor nerves, probably due to exhaustion, degenerative changes, or inefficient nutrition, is followed by a reduction of blood-pressure. More important than the disturbance of blood-pressure, although no doubt largely due to the same, is the *change in the blood distribution;* the latter in fever often varies greatly, as already referred to when considering the dissipation of the abnormal heat. The large glandular viscera are not infrequently perceptibly altered by the increased amount of blood sent to them, and its relative, if not absolute, stagnation in their interior.

Blood Changes.—The blood is materially lessened in nutritive value, partly as a result of the interference with assimilation, both primary and secondary, and partly from the destruction of the blood elements. The hematolysis is not usually

manifest until the fever subsides, not having been marked previously by reason of the concentration of the blood, so that a blood examination during the height of the fever fails to disclose the loss of globular elements until, by dilution, after the fever has disappeared, the oligocythemia and oligochromemia become apparent.

Changes in Organs.—In addition to the changes in the blood, other tissues show marked alteration. The large glandular viscera, particularly the liver and kidneys, show cloudy swelling; a similar change occurs in the muscles, the heart often manifesting the granular alteration of its fibers to the highest degree. Hyaline change in the muscles has also been observed. The adipose tissues sooner or later show wasting, and the nerve elements evince the granular and pigment alterations incident to exhaustion. The mucous membranes, that of the alimentary canal in particular, show granular and fatty changes. Many of the tissue changes may arise from contact with the poisons circulating in the blood, others are possibly due to the accompanying elevation of temperature and associated disturbances of nutrition.

QUESTIONS.

(1) What is the normal temperature of the human body? (2) What rhythmic variations occur in health? (3) At what hours of the day do the maximum and minimum temperatures occur? (4) What is meant by (*a*) thermotactic center, (*b*) thermogenic nerves, (*c*) thermolytic nerves, (*d*) thermo-inhibitory nerves? (5) Name conditions in which subnormal temperatures occur. (6) What is the most frequent cause of subnormal temperature? (7) What is pyrexia? (8) What constitutes hyperpyrexia? (9) What is the most frequent cause of fever? (10) What is an intoxication? (11) To what are the microbic intoxications due? (12) Give examples of pure intoxications. (13) What is septic intoxication? (14) What is meant by the term pyrogenous? (15) What hypotheses may be advanced to explain the subnormal temperature of brain abscess? (16) What intoxications may occur without bacteria? (17) What is an auto-intoxication? (18) What is copremia? (19) What

is presumed to be the pyrogenous material in aseptic surgical fever,—for example, after a fracture of the femur? (20) How does this fever differ from a pure intoxication? (21) What is local infection? (22) How may systemic symptoms be produced by a purely local infection? (23) Can the toxins of bacteria produce lesions elsewhere than at the site of the microbes? (24) What is meant by (*a*) primary infection, (*b*) mixed infection, (*c*) secondary infection? (25) Is there any danger from infection by saprophytes? (26) What is a mycosis of the blood? (27) Give an example. (28) What is septicemia? (29) What is pyemia? (30) Explain the production of a metastatic abscess. (31) Give causes of rigors. (32) Give pathology of the process. (33) How does it usually terminate? (34) What is meant by (*a*) intermittent fever and (*b*) remittent fever? (35) How explain the rhythmic or cyclic character of certain fevers? (36) What circulatory phenomena accompany fever? (37) What blood changes occur in fever? (38) What changes occur in viscera?

PART III.

SPECIAL PATHOLOGY.

SPECIAL PATHOLOGY.

CHAPTER I.

BLOOD.*

The circulating **normal blood** consists of a fluid portion, the liquor sanguinis, in which is suspended the solid elements, the blood-corpuscles or blood-cells. The liquor sanguinis is probably identical, or practically so at least, with that circulating medium outside the blood-vessels in the primitive lymph-spaces, and which passes from there to the lymph-glands and back into the circulation. As a part of the blood, it is more than a mere vehicle for the transportation of the solid elements, and with its complex chemistry is the essential food-carrying body to the tissue at large. It is composed of the elements out of which the serum and fibrin may be formed, and while this separation is largely a death change, still evidence is not wanting to show that fibrin formation may be an essential element in the protection of the organism and in repair. Thus the distinct wall of the fibrin, which forms around infected areas or covers an infected serous surface as a pleura, and through which osmosis and the absorption of bacterial products is reduced to a minimum, acts not only as a scaffold upon which embryonic and eventually granulation tissue can build the framework which is to repair the injured part, but, also, as a prophylactic, limiting membrane, through which infection travels only with the greatest difficulty. Again, of all the tissues produced within the body, fibrin offers the greatest

* For technic of blood examination see part I.

resistance to many of the injurious incidents to which the tissues are liable; the constant pressure of the circulating blood, as in an aneurysm, may lead to atrophy and the disappearance of bone, unless conditions arise which determine the intervention of a wall of fibrin through which, not uncommonly, we may hope for a cure. The exact factors which enter into the chemistry of fibrin formation are not known; although the third corpuscle would seem to bear some causative relation to fibrin formation, the character and extent of such influence remains one of the unsolved problems of physiologic chemistry. An excess of fibrin, or fibrin-forming elements, constitutes **hyperinosis,** a condition present in pregnancy.

In addition to the fibrin-forming elements, the serum contains albumin salts and water, all of which constituents are likely to vary within certain limits.

The so-called solid constituents of the blood are the corpuscles, the red, or *erythrocyte*, the white, or *leukocyte*, and the third, blood-plates, or *hematoblasts*. Each cubic millimeter of normal blood should contain between 4,000,000 and 5,000,000 red blood-cells, 6000 to 10,000 leukocytes, 18,000 to 250,000 of the hematoblasts. When a blood count is given, without stating the amount of blood, it is always meant that the number of cells stated were present in one c.mm. of blood.

When considering the technic of blood examination, the varieties of blood-cells were described and their differentiating points given, and while such description properly belongs here it was inserted with the technic for convenience in demonstrating methods (see p. 82).

Held within the cytoplasm of the red blood-cell, under normal conditions, is the blood-coloring matter, the *hemoglobin*. The normal amount of hemoglobin is between 13 gm. and 14.5 gm. approximately, to each 100 c.c. of blood. As ordinarily expressed by the instruments now in use, the reading is given in percentages of the normal; thus, a hemoglobinometer

reading 70 per cent., means 70 per cent. of the normal or an actual amount of hemoglobin amounting to 9.8 gm. to 100 c.c. of blood, presuming that the normal is 14 gm. to 100 c.c.

Anemia (by reason of their relation to certain phenomena in general pathology, plethora, anhydremia, etc., were there defined. See page 137) is a term broadly used to mean bad blood. It implies a reduction of any one or more of the essential elements of the blood. Anemia is said to be *general* or *local;* the latter has been considered (see p. 135).

General anemia may be *primary* or *secondary.* By the former is implied an anemia due to lesions or disorders of the blood-making or hematogenic organs, or abnormal blood destruction, excessive hemolysis.

Some authors regard as **primary** or **essential anemias** only those due to deficient blood making, a view having strong reasons for support, but not fully acceptable until we establish that pernicious anemia is not due to excessive hemolysis. Among the primary anemias we may class *chlorosis, pernicious anemia, leukemia* or *leukocythemia, Hodgkin's disease* or *pseudoleukocythemia* or *pseudoleukemia*, and *splenic anemia.*

In some of these we have pronounced reduction of the coloring-matter of the blood, a condition known as **oligochromemia.** The amount of hemoglobin may fall to less than four grams in the 100 c.c. of blood, a reduction of over 70 per cent. The amount of hemoglobin may be greatly reduced without a corresponding reduction in the number of red cells; in chlorosis the hemoglobin may fall to 25 per cent. of the normal, while the number of erythrocytes may be 4,000,000; it will therefore be apparent that each red cell has but little more than one-fourth of its normal coloring-matter. With the reduction of the hemoglobin, the amount of iron, which forms such an essential part of the coloring-matter, is also reduced. Occasionally, as in pernicious anemia, the number of red cells may be one-half of the normal, while the percentage

of hemoglobin may be practically normal or, more likely, 70 per cent. This is equivalent to saying that the blood contains more coloring-matter than is normal for the number of red cells present, a condition called **hemoglobinemia**; whether such hemoglobinemia is plasmatic, the coloring-matter dissolved in the plasma,—extracorpuscular hemoglobinemia,—or whether the excess of coloring-matter is taken up in the undestroyed cells of the blood,—an intracorpuscular hemoglobinemia,—still remains a matter for speculation.

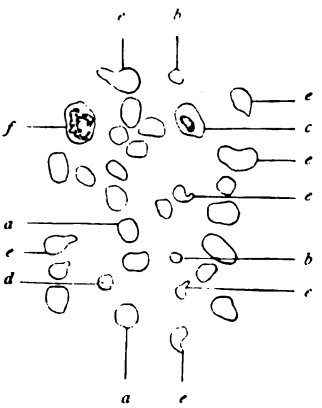


FIG. 224.—THE BLOOD IN PERNICIOUS ANEMIA. (PARTLY DIAGRAMMATIC.)

From a case of pernicious anemia in the Jefferson Medical College Hospital. Redrawn from cut in original article on blood staining by J. C. DaCosta, Jr., M.D., in *Microscopical Bulletin*. *a*, *a*. Macrocyte. *b*, *b*. Microcyte. *c*. Giganoblast. *d*. Normoblast. *e*, *e*, *e*, *e*, *e*, *e*, *e*. Poikilocyte. *f*. Leukocyte.

Oligocythemia is a term applied to the reduction in red blood-cells, a phenomenon present to a variable extent in nearly all blood diseases. In the symptomatic or secondary anemias the red cells are rarely below 2,000,000, while in the essential anemias they may fall much lower. In chlorosis the red cells are but little reduced, the average being 4,096,544, although cases as low as 1,500,000 are not unknown. In pernicious anemia the count may fall, when near the end, to less than 500,000, Henry reporting a case with a count of 315,000. In leukemia the fall is much less marked, the number of red cells rarely going below 2,000,000; much lower counts, have, however, been observed. In Hodgkin's disease the fall is usually not great; counts as low as 1,000,000 are reported.

Not uncommonly, with the reduction in number, the red

cells show most varied shapes, **poikilocytosis, poikilocythemia.** *Poikilocytes* may be spheric or globular, pear-shape, bobbin-shape, crescent-shape, drawn out into fibril-like bands, at the ends of the band a knob-like enlargement,—in other words, all types of irregular or deformed red cells (see Fig. 78, p. 82). It is believed that these represent dying or fragmenting types of the red cell. **Microcytosis** and **megalocytosis** are self-explanatory terms (see "Blood Technic," p. 82). Among the immature or embryonic forms of cells seen in the blood are the *normoblasts* and *megaloblasts*, —nucleated types which are observed in conditions of rapid blood destruction, and supposed to be cells rushed into the circulation before the phenomena of development were completed. These are regarded as constant (pathognomonic by some observers) in pernicious anemia; many observers, however, report some nucleated forms in leukemia.

In addition to the abnormalities of shape and the presence of nuclei, red corpuscles occur in which the cytoplasm and granular contents may show separation without, of necessity, deformity, or nucleation but isolation of coloring-matter; such cells are said to be **plasmoschitic,** and the cell condition is called **plasmoschisis.**

Polychromatophilia is a name applied to a condition in which the blood-cells react in an unusual way to the common blood stains. It is presumed to be a degenerative phenomenon.

Leukocytosis.—The relative number of leukocytes, as compared with the red blood-cells, is 1 of the former to 600 or 1000 of the latter. The range of the white blood-cells is, however, greater than these figures would indicate; as, after a hearty meal, the number of leukocytes may rise to 50,000, that is, 1 white for every 100 red cells. Such a rise is, however, very transitory; a slight rise, more persistent in character, occurs during gestation. These are types of the so-called **physiologic leukocytosis,** recognizable by the transitory

character of the phenomenon, with almost constantly recurring subsidence to the normal, which, however, may not be at any time quite attained. As a rule, no difficulty is found in differentiating the so-called physiologic leukocytosis from pathologic leukocytosis.

Hypoleukocytosis is a reduction of the number of leukocytes below the normal; it not uncommonly precedes leukocytosis, is seen at times in typhoid fever, and is presumed to depend upon a visceral determination of the leukocytes and their temporary lodgment in the capillaries of the large glandular viscera, and particularly the lungs,—a hypothesis without distinctive evidence upon which it can rest.

Pathologic Leukocytosis.—Probably the most frequent form of pathologic leukocytosis is that which accompanies many of the infections, the so-called *inflammatory leukocytosis.* This may reach 1 white to 20 red cells; the newly added leukocytes are, for the most part, of the multinucleated variety. In septic processes and in pneumonia the leukocytes may increase with astonishing rapidity. That this form of leukocytosis bears some relation to the infections can be shown experimentally by the injection of certain bacteria, and that it is due to a poison generated by the bacteria, rather than to the bacteria themselves, is indicated by its production after the injection of sterile cultures. Whether the added white cells are produced in excess by the normal sources; whether they are formed by proliferation in the blood, or are merely thrown into the peripheral circulation by a threatened invasion of their habitat by some noxious agent, remain questions for future study. A leukocytosis arises in connection with certain forms of anemia in children, in which there may be 1 leukocyte for every 15 to 20 erythrocytes; its cause is unknown.

Leukemia represents a form of leukocytosis which differs in many respects from the leukocytosis already described, but is, of course, pathologic. The leukocytes may equal in

number the red blood-cells. The number and percentage of each form is largely dependent upon the type of the leukemia. Admitting the possibility of three types of leukemia,—*splenic*, *lymphatic*, and *myelogenous*,—the fact remains that practically but two forms occur,—(1) the *splenomedullary*, or *lienomyelogenous*, and (2) *lymphatic leukemia*.

In the first, the most frequent form, the lymphocytes are relatively diminished, polynuclear neutrophiles (the normal leukocyte in excess) may be normal or reduced relatively;

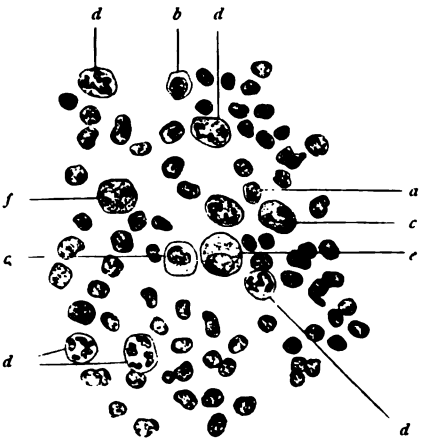


FIG. 225.—THE BLOOD IN LEUKEMIA. (PARTLY DIAGRAMMATIC.)

From a case of splenic myelogenic leukemia in the Jefferson Medical College Hospital. Redrawn from cut in original article on blood staining by J. C. DaCosta, Jr., M.D., in *Microscopical Bulletin*. *a*. Small lymphocyte. *b*. Large lymphocyte. *c, c*. Transitional leukocyte. *d, d, d, d*. Polynuclear leukocyte. *e*. Myelocyte. *f*. Eosinophile.

the large number of myelocytes is the interesting and most characteristic feature. Of 500,000 leukocytes, over 150,000 may be myelocytes. The red cells are not greatly reduced, usually not below 3,000,000. In the lymphatic form of leukemia the leukocytosis is not commonly so marked, the number rarely over one white for ten red corpuscles. The leukocytes in excess are lymphocytes, frequently over 90 per

cent., both large and small occurring. Myelocytes are not present in pure lymphatic leukemia. The red blood-cells are in the same condition practically as noted in splenomedullary leukemia, except that nucleated forms are much less common.

Mixed forms of leukemia are not exceedingly rare; in these we find more or less intermingling of the two forms just described. The differential count of the leukocytes enables one to distinguish leukemia from those cases of Hodgkin's disease in which leukocytosis is present; in Hodgkin's disease only the adult cells are increased. The same differentiating point applies to tumors of the spleen and kidney and other forms of leukocytosis.

In **secondary anemias** the fault lies, not in the blood-making, or excessive blood-destruction as carried on in the usual way, but implies waste of blood or blood-forming elements. Under this head we have the anemias resulting from hemorrhage due to trauma, ruptured aneurysm, hematemesis, hematuria, hemophilia, purpura, and other direct blood losses in which more or less blood leaves the body or becomes extravascular, and therefore of no value in general nutrition. Similarly, anemias due to wasting discharges, suppuration, lesions of organs not directly influencing blood-making, although indirectly so,—as cancer of the stomach,—are secondary anemias; these properly include the *anemia of inanition*, such as occurs from cancer of the esophagus. Certain secondary anemias result from poisons circulating in the blood, and are known as *toxic anemias*. In some of these the blood-destruction may be direct, as in poisoning by carbon monoxid; in others the blood-destruction may be less rapid but even more marked if the cause be permitted to continue long, as in chronic lead, mercury, arsenic, and phosphorus poisoning. The blood-destruction secondary to fever, syphilis, and other infections, both acute and chronic, is classed with the secondary anemias.

Melanemia (pigment in the blood-plasma and leukocytes)

is seen in certain forms and stages of malaria, occasionally in relapsing fever, and, at times, it is alleged, that in melanotic malignant tumors free pigment may be taken up by the leukocytes and carried into the blood. The pigment is rarely found in the plasma, as the leukocytes engulf it as soon as it becomes free. Soluble pigments, as, for example, bile pigments, may be found in the plasma (*cholemia*). Pigmentation of leukocytes is supposed to be an evidence of the pigment having first been free in the blood, but the extravascular existence of the leukocyte admitted, we can understand that the pigment may have been acquired outside of the blood.

Lipemia (fat in the blood) has no clinical significance so far as at present known.

Excessive hematolysis (increased blood-destruction) is seen in certain morbid conditions, as in malaria and yellow fever, less commonly in typhus and scarlet fevers. In profound sepsis, particularly in blood mycoses, rapid dissolution of the cellular elements of the blood may take place. Thus in anthrax, hemoglobinuria is taken as an evidence of the destruction of red cells and the liberation of their coloring-matter which is excreted in the urine. Certain poisons are able to induce rapid blood-destruction: phosphorus, carbon dioxid, and sulphuretted hydrogen may be taken as examples of such poisons.

The influence of hemorrhage on the composition of the blood is believed to be fairly understood. With the withdrawal or escape of blood from the vessels the volume is, as rapidly as possible, made up by the absorption from the tissues at large of available fluid to replace, in volume, the blood lost. This renders the blood hydremic, and is beneficial by enabling the vascular apparatus to maintain the blood-pressure upon which equality of blood-distribution so largely depends. The dilution lessens the corpuscular richness of the blood, the red cells falling, often with great rapidity, until, in

grave cases, less than 1,000,000 may be present. It is possible that the rapid and disproportionate fall of red cells may be partly accounted for by, in addition to their actual removal with the blood in bulk, the well-known fact that rapid and excessive dilution of the blood gives rise to swelling and eventual solution of the red blood-cells. With the reduction of the red blood-cells the hemoglobin proportionately falls; the regeneration of the red cells may go on rapidly, but the coloring-matter is very much more slowly replaced, so that the anemia at first produced is a true oligocythemia, with its necessary concomitant oligochromemia; the former, rapidly in healthy individuals, is replaced by the normal, while the latter resumes the normal but slowly. There is an important practical bearing in the knowledge of oligochromemia, as its extent should have a most careful consideration by surgeons before attempting operations. Cabot credits to Mikulicz the aphorism: "*Never operate on any case when the hemoglobin is below 30 per cent.*"

Quickly following, sometimes almost coincident, with the hemorrage, if it be not too rapid, leukocytosis occurs; the adult or polynuclear leukocytes are most increased, and, although the leukocytosis is never high, the count may reach 25,000 to 35,000.

Mycoses of the Blood. (See "Intoxications and Infections," p. 368.)—The possible infections of the blood may be greater than we at present presume. The organisms of anthrax, tuberculosis, glanders, typhoid, and relapsing fever, also the pyogenic and a few other bacteria, have been identified in the blood. Care must be used in drawing conclusions from the presence of bacteria in the blood postmortem, as it has been, we may say, demonstrated, that in the *agonal period*—the final moments, or it may be hours, of the death agony—bacterial diffusion is favored by the lessening bactericidal action of the blood and the probable increasing permeability of the vessel

walls. The demonstration of bacteria in the blood does not materially differ from their demonstration elsewhere. (See "Bacteriology," p. 242, also "Technic of Blood Examination," p. 78.)

Animal Parasites.—The animal parasites found in the blood are broadly classed as *hæmatozoa*. The most important are the *malarial organism*, the *embryo of the Filaria sanguinis hominis*, and the *Distoma hæmatobium*. The last named is more truly a parasite of certain vessels—the portal vein and its branches and the venous ramifications around the bladder and rectum. (See "Animal Parasites," also "Technic of Blood Examination.")

QUESTIONS.

(1) Give composition and structure of blood. (2) What is hyperinosis? (3) What is anemia? (4) What is primary anemia? (5) Name the primary anemias. (6) What is oligochromemia? (7) What is hemoglobinemia? (8) What is oligocythemia? (9) What is the average number of erythrocytes in (*a*) chlorosis and (*b*) leukemia? (10) What is the condition of the red blood-cells in pernicious anemia? (11) What is poikilocythemia? (12) What immature embryonic cells occur in the blood? (13) What is plasmoschisis? (14) What is polychromatophilia? (15) What are the forms of leukocytosis? (16) How differentiate them? (17) What white cell is most abundant in inflammatory leukocytosis? (18) What is the probable cause of the leukocytosis of infectious diseases? (19) What is hypoleukocytosis? (20) What are the forms of leukemia? (21) How differentiate them? (22) What variety of leukocytes is increased in Hodgkin's disease? (23) What is meant by secondary anemia? (24) Give an example of an anemia of inanition. (25) What causes may produce toxic anemia? (26) What is melanemia? (27) In what conditions is it found? (28) What is cholemia? (29) What is lipemia? (30) Under what conditions may excessive hematolysis occur? (31) What blood changes follow hemorrhage? (32) Mention some mycoses of the blood. (33) What animal parasites may be found in the blood?

CHAPTER II.

SEROUS MEMBRANES.

The **normal serous membrane** is composed of a flattened-out layer of connective-tissue cells (endothelium) resting upon a subserous network of loose connective tissue in which ramify the blood-vessels, lymphatics, and nerves. The membrane produces no secretion, but is lubricated by a transudate of serum which probably passes out between the connective-tissue cells through the open mouths of the lymphatics; these openings constitute what are known as the *stomata* of the serous membranes, and, by making the membrane cavity continuous with the general lymphatic circulation, render the view that the serous cavities are only immense lymph-spaces probably correct. The blood-vessels to the serous membranes are derived from those supplying the organs which the serous membrane covers; it is also probable that the lymphatic system of the serous membrane is intimately associated with that of the subserous tissues. These views, if correct, explain the inflammatory processes which occur on the serous surfaces as secondary to inflammations of the underlying organ—*e. g.*, the pleurisy of fibrinous pneumonia.

The serous cavities of the body are the *peritoneum*, *pleuræ*, *pericardium*, the *serous covering of the brain and cord*, the *synovial structures of the joints and tendon sheaths*, and the *bursæ*. When we examine one of these in its normal condition, we find that it is moist, smooth, shining, and transparent. The color is uniform with that of the tissue which it covers, and where two layers of the serous membrane have nothing between them but the fibrous or fibro-elastic network on which

they rest, it may be practically true that the membrane is colorless. The normal serum of the cavity is a clear fluid, usually of a light straw color; it may, however, be stained by osmosed coloring-matter, as the coloring-matter of the blood, which may pass through the heart postmortem and stain the pericardial fluid. The amount of fluid present in any given serous membrane is dependent upon the amount in the connective tissues elsewhere, as well as the surface area of the membrane in question, and must, therefore, vary enormously. If the patient has died slowly, and a general lymph stasis has ensued from the gradual slowing of the circulation, more fluid will be found in the serous sacs than under conditions of rapid death.

The amount of fluid which can be collected will approximate, in the peritoneum, two to four drams; in the pleura, one to three ounces; in the pericardium, two to six drams.

If, during life, for any reason, there be slowing of the circulation leaving a serous membrane, or the organ which it incloses, there will be a disposition for fluid to accumulate in the serous cavity, just as obstruction to the onward flow of blood, in any part of the body, leads to the infiltration of the lymph-spaces with serum (see "Edema," p. 139). Such an accumulation constitutes what is often spoken of as **dropsy of a serous cavity.** *Ascites*, or *hydroperitoneum*, from obstructive lesions in the liver is an example of this condition. The accumulation of fluid in the pleura (*hydrothorax*), in pulmonary edema and general dropsy, is a second instance; similar conditions may cause *hydropericardium*. The accumulated fluids interfere mechanically with the function of the organs in the cavity at fault, and increase the venous congestion which may have been the original cause.

Accumulations of serum, without any evidence of inflammation, occasionally occur in serous cavities where the membrane is infiltrated by miliary tubercles. The tubercles surrounding

and obstructing the small vessels, arteriole, capillary, and vein, lead to extravasation exactly as any other obstructive lesion. The process is most common in the peritoneum, where not uncommonly gallons of fluid may be, at different times, drawn off, only to re-accumulate, as in the ascites due to obstruction of the portal vein in its distribution in the liver.

The order in which the serous cavities of the body are examined is: (1) Peritoneum, (2) pleura, (3) pericardium, and (4) the serous membranes covering the brain and cord. The processes in each of these, when affected by disease, vary so little, the variation depending not so much upon the membrane as the surrounding structures, that we may study in detail disease processes in one of the cavities and apply that knowledge to any or all of the other serous membranes with but slight modification; *e. g.*, the brain, being inclosed in a rigid covering (the skull), will never be surrounded by the accumulations of fluid so constantly found in inflammations of the pleura. Remembering these variations in the process, as affecting different membranes, we will consider the most convenient serous membrane, namely, the pericardium.

Malposition of the Pericardium.—Whatever malpositions affect the heart, the pericardium will accompany the heart in its abnormal place. As the development of the pericardium is dependent upon the development of the heart, the sac never occurs without its enveloped viscus.

Malformation of the pericardium occurs but rarely, and usually consists of *partial* or *complete absence* of the membrane. Do not be misled by considering a universally adherent pericardium as illustrative of absence of the organ. Normally, the phrenic nerves are widely separated by the pericardium, but in those cases of absence of the pericardium which have been reported, the two nerves are almost side by side. This will, therefore, aid in demonstrating that the pericardium was present at one time and that inflammation sealed its walls together.

"*Milk*" *spots* on the pericardium are occasionally found, and are usually due to the heart thumping, at each pulsation, against some hard body, as a prominent costal cartilage, or, more rarely, the vertebræ. These spots are to be differentiated from the deeper lesions of fibroid change in the cardiac muscle by the former being thin, superficial, not in the muscle, but on its surface. Rarely the spot may be slightly calcareous.

Infiltrations.—Pigment is rarely found in the pericardium. Fatty infiltration is occasionally observed. Calcareous areas may be seen, particularly if the membrane has ever been the seat of inflammation.

Degenerations.—Fatty, myxomatous, hyaline, and granular changes occur, but not frequently.

Inflammation of the pericardium (**pericarditis**) is analogous to inflammation of the peritoneum (*peritonitis*), inflammation of the pleura (*pleuritis*, or pleurisy), inflammation of the meninges (*meningitis*).

Acute Pericarditis.—Clinically, pericarditis is said to be *acute* or *chronic;* pathologically, it would probably be better to refer to it as simple and infective, the simple form being separable into the acute or chronic, the infective depending upon the character of the infection, running a rapid or a prolonged course. As all the infections are not as yet fully worked out, the clinical classification must, at least for the present, be accepted.

Causes.—Injury, cold and exposure (?), rheumatism (about 50 per cent. of the cases), gout, septic processes, tuberculosis, inflammations of the kidney—more particularly the chronic form, direct infection, and by extension of inflammation from adjacent structures, *e. g.*, peritonitis, rarely pleuritis, occasionally pneumonia, and extension from the esophagus, as when the latter has been injured by trauma, escharotic poisons, etc.; a foreign body lodged in the gullet may ulcerate into and involve the pericardium. Of the microbic

causes, the organisms of suppuration, the pneumococcus, and the bacillus of tuberculosis are conspicuous, although other bacteria have been frequently found.

Morbid Anatomy.—In the first stage the membrane is dry, red and injected, slightly opaque, and much roughened. It may be sticky, and it always presents, over the inflamed area, a dull surface in contrast to the shining luster of the normal. Histologically, at this stage, the subserous capillaries are distended with blood; the areas of capillary hyperemia are scattered over the membrane irregularly, and look as though a smear of carmin stain had been daubed over the surface at irregular intervals; rarely, if ever, is the hyperemic capillary distention universal. The *morbid physiology* is shown in the friction sounds discernible on auscultation, and due to the roughened and dry surfaces rubbing against each other; the pain of this stage is probably due to direct irritation of nerve filaments, and partly to the irritation of the nerves by the application of the chemic bodies engendered by the changes in cell metabolism; it seems not improbable that the fever of this stage is due to the same cause, entering the circulation by resorption.

The second stage is brought about by the blood-vessels relieving themselves of those materials which ordinarily escape in any inflammatory process. The liquor sanguinis escapes from the distended capillaries, and passing through the stomata of the serous surface, reaches the cavity. Immediately upon reaching the surface of the membrane it splits into fibrin and serum, the former coating the surface of the serous membrane, the latter finding room in the cavity. With the transudation or escape of the liquor sanguinis the leukocytes pass by diapedesis directly into the fibrinous and serous exudate. It is also probable that the flattened connective-tissue cells are to some degree detached. Should the exudate be slight, the serum rapidly absorbed and but little

remain in the cavity, clinically, the inflammation is spoken of as *plastic* or *fibrinous*; if, however, the exudate be abundant, the serum not taken up, the process is spoken of as *sero-fibrinous*. Presuming to call the first stage the stage of engorgement or hyperemia, the appearance of the exudate initiates the stage of exudation.

In this stage, the membrane will be found either partially or completely covered with fibrin, the degree of cohesion being dependent upon the thickness of the layer and upon its age, as we shall see presently. The serum in the serous sac will differ from the normal in that it will be opaque and contain flocculi of fibrin, the opacity being due in part to the fibrin, but largely to the abundant presence of leukocytes. The soft, downy mass of fibrin hanging in shreds has given to the heart, at this stage, the name, *cor villosum*. The thick, shaggy layer of fibrin may remain adherent to the membrane, or the fibrin may be whipped off to a greater or lesser degree by the movements of the inclosed organ. The *morbid histology* of this stage will be found to be a reduction in the size, and a less crowded condition, of the subserous capillaries, they having largely relieved themselves by unloading themselves of those materials which have gone to form the exudate; the layer of fibrin, on section and in teasings, will show the abundant presence of leukocytes and a few red cells, while the endothelial cells will be seen to be desquamating, the process at points being laminated, masses of these elements being discernible far up in the fibrinous layer.

The *morbid physiology* of this stage is shown in resistance offered to the functional activity of the encumbered organ. If an abundant exudate be present, pressure will influence the action of the environed organ and mechanically impede its function. Friction sounds disappear if the exudate be sufficient to force the two layers apart and the fibrin covers the roughened serous surfaces. The fever may be kept up by

the absorption of the metabolic products; these also induce, not uncommonly, phenomena not usually due to pyrexia alone—*e. g.*, suppression of excretion and certain nervous symptoms. The fibrinous exudate may so conceal and obstruct access to the lymphatic and vascular exits as to preclude absorption of the serum or its pyrogenous constituents, and so no systemic phenomena due to their absorption may be manifest. Where percussion and auscultation can be brought into play, the phenomena associated with the presence of solid or liquid materials may be found—*e. g.*, dulness.

Exactly how long these two stages may last can not even be inferred; their duration varies, the condition inducing the variation being but poorly understood; the cause, the severity of the attack, the condition of the patient, whether weak or strong, are undoubted determining factors. The stages may be prolonged or brief, and just what determines this can not always be definitely stated; sooner or later, if the patient survives, repair proceeds as follows:

In this stage the leukocytes and the connective-tissue cells present in the wall of fibrin proliferate and convert the layer into embryonic tissue, young blood-vessels are developed from the subserous layers, and lymphatic connection is re-established. The rapidity with which young blood-vessels shoot up into the new tissue is marvelous, and to the rapidity with which this process of organization develops, modern surgery owes much of its great achievements. The proliferated leukocytes and young connective-tissue cells, the progeny of the endothelial lining, constitute a small, round-cell mass known as embryonic tissue; when the young blood-vessels permeate this structure,—in other words, when it becomes vascularized,—it is known as granulation tissue. The next step is the organization of this into fibrous connective tissue, which, becoming smoothed, gives a surface functionally normal as far as the

surface is concerned, but as all organizing tissue manifests a tendency to contract, grave results may ensue in the tissues beneath. Pressure upon nerves leaving the brain may, by constriction, lead to their entire loss of conducting power, paralyses, blindness or deafness being thereby produced. Over the lung the contraction may preclude re-expansion and favor the continued presence of the serous exudate. A band around the intestine may cause obstruction. In the pericardium, however, it is not believed that the contraction does sufficient harm to merit consideration.

Adhesions between two layers of a serous membrane—*e. g.*, the pericardium—are brought about by the two fibrinous surfaces coming together at any stage of the inflammation before organization is well under way. In the recent state the fibrinous layer of one side will adhere to its duplicate if they come in contact, and it is not improbable that in the embryonic-tissue stage of the membrane, or even when vascularization is well advanced, cohesion of the two surfaces, followed by an organized adhesion, is possible; after sticking together of the surfaces, the young blood-vessels anastomose and pass from one side to the other, organization into fibrous tissue ensues, and an adhesion is the result. The constant movement of the heart probably precludes the general union of the pericardial layers at a single attack, but in the pleura it is not improbable that the entire sac may be obliterated by a single inflammatory attack. Whether adhesions form or not, the serous membrane remains permanently thickened. Into this new tissue lime salts or fat may be deposited; in the former instance the condition is known as *calcification*, in the latter, *fatty infiltration*.

An opportunity is afforded to study the formation of adhesions in almost all surgical operations upon serous surfaces. A wound of the intestine has the two serous surfaces brought together by sutures; along the line of contact an exudation of liquor sanguinis and the migration of leukocytes occurs;

the former breaks up into fibrin and serum, the fibrin forming a temporary cement which binds the two apposed surfaces together; embryonic tissue is formed, followed by granulation tissue, and later by a cicatrix which binds the surfaces together

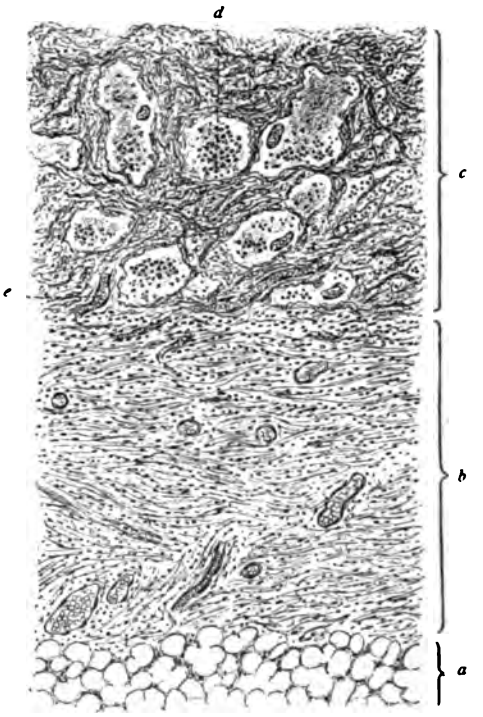


FIG. 226.—VERTICAL SECTION THROUGH AN INFLAMED SEROUS MEMBRANE AFTER THE FORMATION OF THE FIBRINOUS EXUDATE.—(*Schmaus.*) × 250 diameters.

a. Subpericardial fat. *b*. Swollen membrane, the surface of which is continguous to and blends with the overlying fibrinous deposit *c*. *c*. Layer of fibrin in which are numerous leukocytes, *d*, and into which, at *e*, are developing blood-vessels.

along the line of suture. This cicatrix is an adhesion, the histology and mode of development of which is practically identical with the formation of adhesions in pericarditis, pleurisy, inflammations of tendon sheaths, etc. The closing or

obliteration of the sac of hydrocele is brought about by inducing an inflammation of the serous membrane and favoring adhesion of the walls by withdrawal of the contents, thereby permitting collapse.

Suppurative pericarditis results from the infection of the serous membrane by pyogenic bacteria. Whether these were present from the beginning, as after a wound of the pericardium, or whether infection followed the initial processes, matters but little. The peptonizing influence of these organisms manifests itself as soon as the development of embryonic tissue occurs; this is liquefied as rapidly as produced, and pus is thereby engendered. Vascularization is impossible while the process of liquefaction is going on, and the interminable persistence of the process has given the infected membrane a name descriptive of its pus-producing characteristic, it being known as a *pyogenic membrane*. In the suppurative inflammation of serous membranes the fever-producing element present in the non-infective forms has its activity augmented by the addition of the pyrogenous products of bacterial life (see p. 365). The accumulation of pus in the pleura constitutes what is known as *empyema* or *pyothorax;* in the pericardium, *pyopericardium;* in the peritoneum, *pyoperitoneum*, *peritoneal abscess*, *suppurative peritonitis*, etc.

Chronic pericarditis consists in the presence of the results of the acute form, and is thus known as adhesive or adherent pericardium. The condition present may be that of: (1) Partial or complete adhesion; (2) large masses of fibrin whipped off in the serum may not have undergone absorption, but remain as caseous or semisolid collections too large to be vascularized; (3) caseous areas resulting from the absorption of the fluid portion of a past pus collection or tuberculosis of the membrane; (4) calcareous masses in the newly-formed inflammatory tissues. Where these forms exist, the only

morbid physiology which is likely to be present will be increased work for the heart.

Tubercular inflammation of the pericardium or other serous membrane may exist in two forms, acute and chronic. The source of the infection is usually tuberculosis of some organ or tissue adjacent, as mediastinal tuberculosis and tuberculosis of the lungs, acting as causes of tubercular peri-

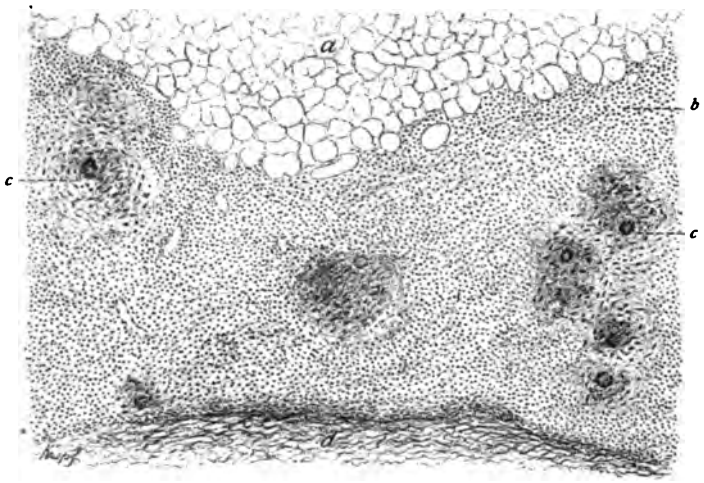


FIG. 227.—ACUTE TUBERCULAR PERICARDITIS, VERTICAL SECTION OF INFLAMMATORY EXUDATE.—(*Schmaus.*) × 250 diameters.

a. Subpericardial fat. *b*. Layer of granulation tissue which extends to the layer of fibrin, *d*. *c*, *c*. Tubercles containing giant-cells. Other tubercles are shown, in some of which degenerative changes are beginning to evince themselves.

carditis and pleurisy respectively. Tuberculosis of the middle or internal ear may cause tubercular meningitis. Tuberculosis of the alimentary canal or mesenteric lymph-glands may be followed by tuberculosis of the peritoneum. Again, tuberculosis of any one, it may be two or more, serous cavities may occur as a part of an outbreak of acute disseminated miliary tuberculosis (see "Tuberculosis," p. 234). In acute tubercu-

losis of a serous membrane, the phenomena described when considering acute simple pericarditis will usually be found present; the same fibrin layer and serum will be found, and only after the most careful search may the tubercular origin of the process be demonstrable, as tubercle bacilli are rarely present in the serum, but may occasionally be found in the fibrin layer; at times distinct miliary tubercles may be found in the new tissue or in the membrane beneath; when, however, miliary tuberculosis exists in a serous membrane, sections, or occasionally stripping, will usually show the presence of the tubercles.

Inflammation of the serous membrane is sometimes accompanied by a hemorrhagic exudate; at such time the term **hemorrhagic inflammation** is used. It occurs most commonly in connection with debilitating conditions, such as tuberculosis, asthenic states, cancer of the serous membrane, and, rarely, without any apparent cause. Trauma may lead to hemorrhage in the exudate. Tapping may rupture some of the delicate vessels of an organizing exudate, or the withdrawal of the serous exudate so remove the support to the delicate newly-formed capillaries, which may rupture, and thus give rise to blood in the fluid. The hemorrhagic phenomenon may show in the serum, or it may exist as petechiæ or areas of subserous rhexis.

Infections in the serous membranes not included in the above list occasionally occur. **Actinomyces, glanders,** and other bacterial chronic infections may occur.

Aside from the ordinary pyogenic organisms which may invade a serous cavity, it would seem that the *Micrococcus lanceolatus* may occasionally cause inflammation of the intrathoracic serous cavities, and the *Bacillus coli communis* is, no doubt, the exciting cause of many of the inflammations occurring in the peritoneum. In the female, extension from the genital organs affords opportunity for ingress of many

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microbic infections, such as the gonorrheal and suppurative peritoneal inflammations in the pelvic peritoneum.

Air in serous cavities has long been recognized as a dangerous occurrence, and gas or air in the sac of the peritoneum has long been considered as a certain precursor of suppurative processes. The reason is apparent: all sources of air ingress mean infection, the import of which need not be explained. Air or gases in the pericardium (**pneumopericardium**) may occur as the result of wounds of the chest wall, ulcers of the esophagus and stomach, or wounds of the former made from within, as by foreign bodies, bougies, etc. In the large majority of cases in which air is found in the pericardium it entered post-mortem; in raising the sterum, the least puncture, so small as to be undetectable, may permit air to enter the pericardium. By remembering this possibility, one is not likely to be misled.

Blood in the pericardium (**hemopericardium**) may follow rupture of the heart or the first part of the aorta, cancer of the pericardium, rupture of the pulmonary artery or veins, or a trauma which injures or lacerates the parietal pericardium. The quantity may be slight or excessive.

In scurvy, pernicious anemia, blood mycoses, purpura, phosphorus poisoning, leukemia, and allied conditions, the serous membranes may be studded by pinhead-like dots of subserous hemorrhage, petechiæ.

Hydropericardium may accompany dropsy from any cause. (See "Dropsy of Serous Cavities.")

Inflammations of the serous membranes are spoken of as *localized* or *circumscribed* when the entire membrane is not at fault, as *general* or *diffused* when the process invades an entire cavity. Localized peritonitis is common, localized pericarditis probably never occurs. *Diaphragmatic pleuritis* is a localized inflammation of the pleura at the base. Where the localized process is accompanied by the development of a walled-off

fluid accumulation, the inflammation is said to be *encysted;* rarely such inclosed masses, when they contain pus, are referred to as abscesses,—*e. g.*, of the pleura or peritoneum. They are not truly abscesses, but purulent accumulations in existing cavities.

Tumors of the serous membranes may be primary or secondary. The primary tumors must, of necessity, be of the connective-tissue series, and nearly all the members of this group have been found in the serous cavities and springing from the serous membranes. For some odd reason not known, the omentum seems to be the most common seat of this class of the non-malignant or adult-tissue type of the connective-tissue series: myxoma, lipoma, fibroma, chondroma, and even osteoma may occur. The embryonic connective-tissue tumors, sarcomata, are not infrequent in the serous membranes. Quite a number of sarcomata of the omentum and mesentery have come to the writer's notice. The cancers or carcinomata are always secondary, as they never rise in a pure connective tissue. The carcinomata of the uterus and alimentary canal not uncommonly invade the peritoneum, multiple nodules of secondary cancer developing on the serous surface. Cancer of the esophagus, stomach, or mediastinal glands may invade the pericardium direct or by metastasis.

Of the **cysts,** dermoid may occur in the cavity of the pelvis. Purely *serous cysts* have been noted, but their pathologic significance has not been definitely determined. *Hematomata* in the serous cavities are not of infrequent occurrence, especially in the peritoneum. The blood mass may be absorbed, it may be walled in by inflammation or a laminated circumferential clot; occasionally it may become infected. In the first instance, but little evidence of its presence may in time remain. At other times absorption may be accompanied by clotting and organization of the fibrin, leaving a permanent tumor.

The laminated circumferential clot may organize and inclose a cyst containing the more or less disintegrated blood.

Parasites in the Serous Cavities.—*Echinococcus* or *hydatid disease* has been observed in all the serous cavities. *Cysticerci* are at times met with in serous cavities, but give rise, in most cases, to no discernible disturbance. *Trichinæ* may be found in experimental *trichinosis* in the serous cavity, but I have no knowledge of their occurring in the ordinary form of the disease. They probably never induce any disturbance of the serous membrane. Grosser parasites, such as round worms, have been found in the peritoneal cavity associated with a fulminating inflammation, suppurative in character, infection having occurred as the result of the opening in the mucous membrane which permitted the escape of the worm.

QUESTIONS.

(1) What is the appearance of a normal serous membrane, and what is its structure? (2) How is it lubricated? (3) Is that fluid a secretion or a transudation? (4) Name the serous membranes. (5) What are the malformations of the pericardium? (6) How differentiate between a universally adherent pericardium and absence of pericardium? (7) What are the first evidences of an inflammation of a serous membrane? (8) How do you know that the tissue is hyperemic? (9) Clinically, what phenomena do you find in the dry stage? (10) What immediately follows this? (11) What do we find in the blood-vessels in this stage, and what changes occur in the intravascular contents? (12) Of what is liquor sanguinis composed? (13) What happens to the liquor sanguinis when it reaches the surface? (14) Where would you look for the fibrin? (15) Where does the serum go? (16) How does that serum differ from normal serum? (17) To what is the opacity due? (18) What are the clinical phenomena of this stage? (19) What is the cause of the fever which occurs in the earlier stage and in this stage? (20) What are those products called which produce this fever? (21) What is the next thing that happens, provided resolution takes place? (22) By what is the serum taken up? (23) What changes ensue in the fibrin? (24) How is embryonic tissue converted into granulation tissue? (25) What becomes of the granulation tissue? (26) How is an adhesion

formed? (27) What infiltrations may take place? (28) What do you mean when you speak of a chronic inflammation of a serous membrane? (29) Suppose, at postmortem, you find a large mass of caseous material in the pericardium, to what may it be due? (30) Is there anything besides the remains of fibrinous exudates which may give you a cheesy mass in the pericardium or elsewhere? (31) What is the cause of suppurative inflammation of serous membranes? Name the most common germs. (32) How do these organisms act? (33) How is suppuration produced in the serous membranes; in other words, what is the process by which liquefaction of the embryonic tissue takes place? (34) If this process has gone on for a long time, what changes do we find? (35) What is that thickened membrane called? (36) What are the most common organisms which produce suppuration of the pleura? (37) In the peritoneum, what other organisms are occasionally found? (38) What complications may arise as the result of contraction and adhesion in a serous cavity? (39) What influence does this pulling-in have on the heart? (40) What changes may the contraction bring about in the abdominal cavity? (41) In inflammation of the serous covering of the brain, how do you know there are contractions or adhesions? (42) Under what conditions may dropsy of a serous cavity develop?

CHAPTER III.

VASCULAR SYSTEM.—HEART.*

Normal Structure.—The heart is essentially a hollow muscle divided by partitions into two distinct sides, not communicating with each other; each side is further divided by a perforated septum into two cavities, known respectively as an auricle and a ventricle. The opening through which the auricle communicates with the ventricle on either side is known as the auriculoventricular opening or orifice, and is guarded by valves which open toward the ventricle; on the right side the valve is known as the tricuspid, on the left as the mitral. The right ventricle communicates with the pulmonary artery and the left ventricle with the aorta, the two orifices being guarded by valves opening toward the vessels. These valves are each composed of three cusps, crescentic or semilunar in outline, and known as the semilunar valves of the pulmonary artery and of the aorta, respectively. The exterior of the heart is covered by the pericardium, to which we have already referred (serous membranes), and the interior is lined by a flattened layer of connective-tissue cells (endocardium) applied almost directly to the cardiac fiber, with but little, if any, loose connective tissue intervening; the valves are composed of two layers of the endocardium, reinforced by fibrous tissue, in which are a few elastic fibers. The valves of the right side, having less work than those of the left, are much the thinner, containing relatively less fibrous tissue. The endocardium, including most of the tissue which enters into the forma-

* For method of removing the heart and completing its dissection see page 25.

tion of the valves, is non-vascular, probably receiving its nutrition from the blood flowing over it. The cardiac muscle is of the striped variety, but differs from voluntary striped muscle; the fibers have no sarcolemma, and inosculate by branched filaments, passing from one fiber to another; there is no bundling of the fibers, and the individual fibers are smaller than those of the purely voluntary muscle.

Size of Normal Heart.—The heart is about the size of the fist of the individual; its weight in the male varies between 285 gm. and 450 gm. (10 and 16 ounces), with a mean between 340 gm. and 375 gm. (12 and 13 ounces). The heart of the adult female weighs between 200 gm. and 400 gm. (7 and 15½ ounces), mean between 285 gm. and 300 gm. (10 and 11 ounces). The taller the individual, the heavier the heart. The left ventricular wall is about 1.25 cm. (½ of an inch) in thickness, the right about 0.4 cm. (⅛ of an inch). The ventricular wall is thickest at its middle, next at base, and thinnest at apex.

DIAMETERS OF CARDIAC ORIFICES.—(*After Hamilton.*)

	Male.			*Female.*		
	Greatest.	Least.	Average.	Greatest.	Least.	Average.
	Inch	Inch	Inch	Inch	Inch	Inch
Aortic, ...	1.3	.9	1.	1.	.8	.9
Mitral, ...	1.8	1.1	1.4	1.5	1.	1.2
Pulmonary Artery,	1.5	1.	1.2	1.3	1.	1.1
Tricuspid, . . .	2.2	1.3	1.8	1.7	1.4	1.5

The taller the subject, the larger the orifices.

MALPOSITION OF THE HEART.

(A) CONGENITAL.

(1) **Cervical Heart.**—Heart in the neck; the condition may be complete or partial, and is more frequent in the lower animals than in man.

(2) **Abdominal Heart.**—Through faulty development of

the diaphragm the heart may sink into the abdominal cavity; occasionally the diaphragm does not develop immediately under the pericardium, and where the heart can not sink through the opening, an abdominal viscus may partly pass through into the pericardium, as a result of the difference between the pressure within the two cavities.

(3) **Pectoral Heart.**—The heart may be developed anterior to the chest wall; the wall may be absent, or it may have developed behind the malplaced heart; in rare instances there may be no pericardium, and in extremely rare cases the heart may be extracorporeal,—*i. e.*, outside the body,—the integument having partly closed behind it. Such conditions are not compatible with life, and are usually associated with fissural malformation of the thoracic and abdominal walls.

(4) **Dexiocardia.**—A heart on the right side is compatible with life, and is recognized by insurance companies as not in any way, of necessity, increasing the risk. Vehsemeyer states that but 20 cases of pure dexiocardia have been reported up to March 18, 1897.* It is usually associated with transposition of the abdominal viscera, the liver going to the left side, etc., the combination of transposed organs being known as the *situs inversus.*

Any one of these malpositions may be partial or complete, no two cases being equally marked.

(B) ACQUIRED MALPOSITION.

The heart may be displaced by pressure applied by neighboring or adjacent organs—*e. g.*, by hydrothorax pushing the organ toward the unaffected side; under this head come the malpositions due to aneurysm and mediastinal disease.

Emphysema of both sides pushes the heart downward; emphysema of one side forces the heart to the opposite side.

* *Deut. med. Woch.*, March 18, 1897.

Pleurisy, with contraction or a contracting fibroid pneumonia, may pull the heart toward the affected side. Hypertrophied hearts have their axes more nearly parallel with the axis of the body and nearer the median line.

MALFORMATION OF THE HEART.

(1) **Walls including the septa:**

(*a*) Single cavity.

(*b*) Arrest of cardiac development with a single auricle and a single ventricle, a condition permanent in the chelonia and scaly reptiles.

(*c*) Single auricle with perforate septum between the ventricles.

(*d*) Single auricle with perfect ventricles or a patent foramen ovale, an attempt at closure of the septum between the auricles.

(2) **Blood-vessels:**

As in intra-uterine life the vessels are developed from five branchial arches, it is possible to have innumerable malformations of the great vascular trunks. The following are most frequent:

(*a*) *Patent septum* between the pulmonary artery and aorta, a condition permanent in the crocodile. The aorta and pulmonary artery developing from a single trunk renders the condition possible.

(*b*) *Transposition of the vascular trunks*, the pulmonary artery arising from the left heart and the aorta from the right.

(*c*) *Double aorta:* In development there are two primitive aortæ, a right and a left; ordinarily the right disappears, but it may not do so.

(*d*) *Patulous ductus arteriosus.* Where a stenosis of the pulmonary artery develops before occlusion of the ductus arteriosus, the communication between the aorta and pulmonary artery may remain permanent. There is little difference be-

tween this and *a*, except the location, the latter being immediately at the heart.

(3) **Valves.**—These being developed from the endocardium, may be in excess as to number of leaflets, or the reverse ; the leaflet may be redundant or deficient. Care must be taken not to confuse the results of antenatal endocardial disease with malformations.

Hypoplasia of the heart occurs. The organ is small—may be less than one-half the normal size and weight—and usually has proportionately small vessels. The vessels may be hypoplastic without the heart showing marked abnormality.

General atrophy of the heart occurs as the result of general wasting with or without lessened work, the organ being very much decreased in size and weight. A specimen in the writer's laboratory weighs less than three ounces.

Local atrophy of the heart occurs in the left ventricle and is probably a result of disuse. A stenotic mitral orifice permits but little blood to flow into the left ventricle and gives it but little work. The nutrition is also in most cases below the normal. The condition is usually accompanied by an excessive dilatation of the right side, which may also show hypertrophy.

Brown atrophy of the heart is due to persistent congestion of the muscle, and is associated with old age, inanition, and allied conditions. The organ is of a dark chocolate or maroon color, hard and tough, diminished in size and weight, with tortuous vessels and wrinkled endocardium, due to diminution in surface. Hematoidin or hemofuchsin is deposited in the muscle cell as a granular pigment, near the ends of the nucleus (polar pigmentation) ; the fiber is shrunken, and there is also, probably, a numerical decrease.

Hypertrophy will be considered after valvular disease (see p. 421).

Fatty infiltration of the heart occurs in general obesity ;

after the permanent changes incident to pericarditis ; in chronic alcoholism ; occasionally, in the aged and the insane. There is enormous increase in the subpericardial fat ; fat cells infiltrate between the muscle-fibers, and probably incommode their action. Some believe that atrophy of the fiber may be induced ; this is not probable, as the fibers in the mass are, usually, normal histologically. The condition is sometimes spoken of as *lipomatosis of the heart.* One should not forget that this condition constitutes a most frequent cause of sudden death, the overcrowded muscular fibers failing to contract, or the fat, having penetrated between the muscle-fibers, may have weakened the interlacing network and rupture has ensued.

Albuminoid or amyloid infiltration of the heart may occur in the blood-vessels of the heart, and in the muscle-fiber. The heart is undernourished and anemic ; milky opacity of the endocardium of the right auricle is usually the most common naked-eye phenomenon, although any of the cavities may exhibit the change. It responds to the usual stains, but can rarely be detected except by the microscope.

FIG. 228.—GRANULAR DEGENERATION (CLOUDY SWELLING) OF CARDIAC MUSCLE-FIBER.
—(*Schmaus.*)
The change here is so advanced as to be practically a fatty degeneration, although oil-drops have not as yet appeared in the fiber.

Calcareous infiltration of the heart may occur around the auriculoventricular orifice, usually of the left side, in the valves, in the heart muscle, and under the pericardium. If any of these structures have been inflamed, infiltration of the inflammatory products with lime salts is likely to ensue.

Pigmentary infiltration of the heart.—By some, brown atrophy is considered as a form of infiltration and described under this title.

Granular degeneration of the heart, or **cloudy swelling,** is probably an initial stage in a form of fatty degeneration. It

occurs in infectious processes, such as septicemia, erysipelas, and typhoid fever; in hyperpyrexia, as that of thermic fever; and in exhausting diseases generally, such as pernicious anemia. The heart muscle is softer than normal, feels slightly edematous, is grayish and cloudy, in striking contrast to the bright red of the normal. The muscle cells are more or less loaded with granular debris, albuminoid and not fatty, at this stage, as is shown by the granules clearing up when treated with acetic acid, and not being soluble in alcohol or ether.

Fatty degeneration of the heart occurs: (1) As a general process invading the whole heart or the whole of one ventricle; (2) secondary to some other local lesion, and restricted to a small area; (3) due to poisons, as phosphorus.

(1) *Diffuse or General Fatty Degeneration of the Heart.*—This form arises from the same causes as, and is probably merely a later stage of, granular degeneration. The papillary muscles, or columnæ carnæ, show the change to the best advantage; they are light brown in color, and running across them are yellow striæ, giving them a brindled appearance; at times the muscle is pale yellow rather than brown, at other times brownish-yellow; in the cut wall the fiber lines just below the pericardium are lost, and the tissue appears, as a rule, uniformly yellow. Looking through the pericardium the muscle shows yellow and red striæ, the latter being the unaffected fibers. Under the microscope the affected fibers are loaded with minute oil globules not larger than a red corpuscle. These differ from granular fibers in that the fat stains with osmic acid, and may be dissolved in ether.

The termination of the granular and fatty metamorphoses is likely to be the same,—(*a*) sudden syncope and death from failure to contract; (*b*) gradual failure by reason of increasing incompetency to maintain the circulation. Rupture of the heart is not common in diffuse or general fatty degeneration of the organ, as it has no[illegible]scula[illegible]er to so raise the

intracardiac pressure as to endanger its weakened walls. It is probable that, in the granular stage, regeneration and recovery may ensue; this becomes less likely as the fatty stage advances.

(2) The second form of fatty degeneration is sometimes spoken of as partial or *local*. It is due to a local ischemia, such as would result from atheroma, calcification, embolic plugging, or thrombosis of some branch of the coronary arteries, which are, to a certain extent, terminal. There is a softened spot in the ventricular wall, pale yellowish-brown in color, sometimes greasy to the touch, and occasionally containing oil globules, visible macroscopically. Microscopically, the changes already described are more marked than in the general variety, as the patient usually lives longer, and the small local focus advances further. The process may be followed by: (*a*) Rupture, which is rare in the general degeneration; (*b*) aneurysmal bulging; (*c*) fibroid processes may convert the mass into cicatricial tissue; (*d*) the area may be so small as to give no determining phenomena.

(3) The third form of fatty degeneration,—that due to poisoning,—*toxic degeneration of the heart muscle*, results most commonly from phosphorus, but occasionally from arsenic and antimony. It presents the changes already given, and responds to the general stain and chemic tests of the ordinary fatty degeneration; if an opinion is to be given in a suspected poisoning case as to the presence or absence of fatty degeneration, it must be formed, if it is possible to form such an opinion, while the tissue is fresh.

Hyaline degeneration of the heart differs from the albuminoid or granular change in that the heart muscle-fibers are converted into a hyaline, vitreous substance like the vitreous change in other muscles known as Zenker's degeneration, which occurs in typhoid fever. When present, hyaline degeneration has been discovered by the microscope and not by macroscopic

evidences. In hyaline degeneration the muscle-fibers may be fragmented, the separation of the fragments may be at the junction of the muscle-cells or directly through the cell-wall. When this condition is present, Renaut has proposed the name *segmentary myocarditis.*

Peculiar patches of a yellowish or grayish-yellow color, situated immediately under the pericardium, have been noted. They usually contain bacteria, but not the tissue reactions incident to an infection. The change resembles, in a limited way, an embolic process. Weber regards the condition as a postmortem change in an area of infection, which infection occurred just before death.*

Acute myocarditis is usually infective in point of origin, arising from (*a*) pyemic processes, or, occasionally, in diphtheria, typhoid fever, etc., leading to infected thrombosis of the coronary artery, or, (*b*) spread by contiguity of an infective process from the endocardium or pericardium. Where acute myocarditis does not terminate in suppuration, fatty degeneration, or rupture, it gradually develops the fibroid changes seen in the chronic form.

Chronic, interstitial, or **sclerotic myocarditis** may last for years; it is usually associated with chronic endocardial or pericardial inflammation. It may result from obstructive lesions of the coronary arteries. The muscle-fiber is replaced by fibrous tissue by an inflammatory process; the fibrous tissue may extend through the heart wall, or only partially through; it is hard and tough, usually restricted to the left ventricle and near the apex; it rarely, if ever, occurs on the right side. As a rule, the new tissue is thin, and may gradually relax to form an aneurysm; rarely, however, it may be as much as twice the normal thickness of the heart wall. Simple non-infective embolism of the coronary artery and atheroma

* Weber, *Brit. Med. Journ.*, June 15, 1897, p. 1474.

of the coronary artery and syphilis, are believed to be the most common causes. The disease in its earlier stages is practically a *myomalacia cordis*, although this term is more applicable to areas of softening seen in acute degenerative and inflammatory processes.

Aneurysm of the heart results from any of the preceding

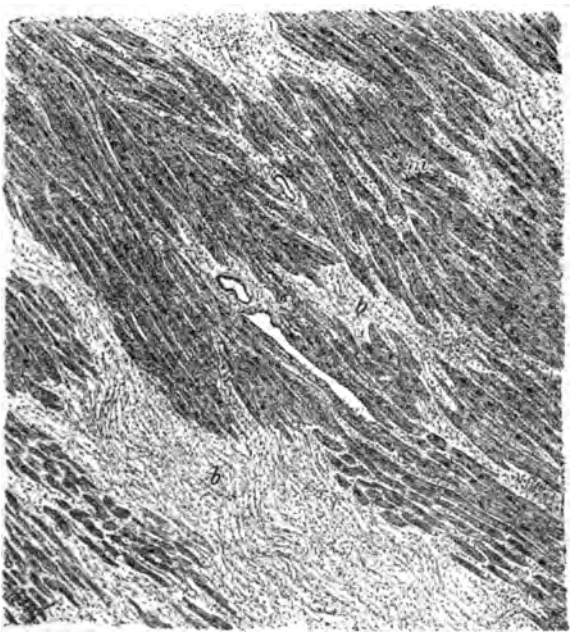

FIG. 229.—CHRONIC MYOCARDITIS.—(*Schmaus.*) × 150 diameters.

m. Cardiac muscle-fibers. *b*, *b*. Newly-formed fibrous connective tissue. This can often be demonstrated to be of different ages, and in the older parts calcareous change may have occurred.

conditions which lessen the resistance of the cardiac wall at any one point. Bulging occurs, the wall of the aneurysm being either a saccular mass without constriction, or a large sac communicating with the ventricle by a small opening. A specimen in the writer's laboratory has a sac as large as an

egg, its wall made up of the endocardium, a layer of fibrous tissue, and the pericardium; the cavity of the aneurysm communicates with the ventricle by a small opening near the apex about one cm. in diameter. Rupture occurs in nearly all cases, and death almost instantaneously follows.

Syphilis of the heart wall usually manifests itself as fibrous or sclerotic myocarditis; some of the cases of fibrous myocarditis are probably cured gummata.

Tuberculosis of the heart may occur; it is usually miliary, and is seen most commonly on the right side, immediately under the pericardium, although the bacillus has been demonstrated in the myocardium and valves.

Tumors of the heart are very rare. The primary tumors are the fibroma, myoma (usually congenital and of the rhabdomyoma class), lipoma, and sarcoma. The secondary tumors are the sarcomata and cancers; the latter can never be primary. Hydatids occur in the heart.

Wounds of the myocardium may not prove fatal even where the heart cavity has been penetrated. Union occurs by a fibrous tissue repair, and not by muscular regeneration. It is probable that regeneration of cardiac muscle is not a possibility, and that the fibroid areas occasionally found postmortem are points at which cicatrization has followed some destructive lesion of the myocardium.

ENDOCARDIUM.

The *normal endocardium* is made up of a flattened layer of connective-tissue cells; a histologic serous membrane. The continuous flowing of blood over its surface, and the difference in function from other serous membranes, render it necessary to describe its diseases separately. The membrane is non-vascular even in its reflected layers, which, reinforced by fibrous tissue, forms the valves; the valves are rich in lymphatics; immediately beneath the endocardium ramifies the

plexus of nerves described by Krause. Recent investigations seem to show that the bases of the mitral and tricuspid leaflets contain some capillary ramifications; the blood-vessels do not, however, approach the free edges of the valves.

INFLAMMATION OF THE ENDOCARDIUM—ENDOCARDITIS.

Sites.—That part of the endocardium having the most work, other things being equal, will first suffer and suffer most. This explains the infrequency of the process on the right side, in adult life, and the rareness of intra-uterine disease of the left side; again, it explains those cases of secondary endocardial inflammation of the right side, in adult life, when extensive obstructive or regurgitant lesion of the left side leads to backing of blood and increased work of the right side. Where the inflammation is in the valvular endocardium, it is known as *valvular endocarditis;* when on the auricular or ventricular wall it is spoken of as *mural;* the latter is rare except in the malignant and atheromatous forms. In the adult, about one-half of the cases of endocarditis occur on the mitral leaflets; of the remaining 50 per cent., about 94 per cent. occur on the aortic cusps; the remaining cases are divided between the valves of the right side, the tricuspid being the more commonly affected.

Forms of Endocarditis:

(A) *Acute* { *Simple.* / *Malignant.*

(B) *Chronic, Indurative, Sclerotic, or Interstitial.*

Acute Simple Endocarditis:

Causes.—(1) Acute articular rheumatism (20 per cent. of the cases). (2) Tonsillitis, which may be rheumatic, and hence involve the first. (3) Infectious diseases of childhood, scarlet fever, etc. (4) Rarely typhoid fever. (5) Chorea. (6) Pneumonia. (7) Diseases associated with general debility and blood dyscrasia, as gout, cancer, diabetes, and inflammations of

the kidney, especially the interstitial form; the last of these acts also by increasing cardiac work. Previous attacks increase the liability to the disease. Various organisms, mostly micrococci, have been found in the valves and exudate, and, while it is not improbable that these exist as a causal factor, the demonstration is not yet complete.

The organisms found include the streptococci, Staphylococcus pyogenes aureus and albus, Micrococcus endocarditidis rugatus (Weichselbaum), Micrococcus endocarditidis capsulatus (Weichselbaum), gonococcus, and the diplococcus of pneumonia; among the bacilli occur the Bacillus pyogenes fœtidus (Passet), Bacillus endocarditidis griseus (Weichselbaum), Bacillus endocarditidis capsulatus (Weichselbaum), and the Bacillus diphtheriæ. Those cases in which the bacillus of tuberculosis has been found are believed to be instances of secondary infection, the bacillus having been implanted upon a pre-existing endocardial lesion.

Heiberg and Winge (1869) first demonstrated bacteria in the lesions of endocarditis. Harblitz* has analyzed the records upon the subject and presumes to differentiate some of the infections by the character of the lesion; streptococcus infections producing large vegetations, the disease progressing slowly and accompanied by nephritis. In the pyemic endocardial lesions containing the ordinary staphylococci, the course of the disease is rapid, the valve destruction great, and associated with more wide-spread infection.

It will be seen that these lesions are a part of the process of malignant endocarditis, and that the microbic factors here considered should be dealt with under that head.

Morbid Anatomy.—This will depend upon the stage. *First stage:* Redness and injection are not present, as the tissue is non-vascular. (*a*) Milky opacity of the membrane, due to

* Harblitz, om Endokardit, dens Pathologiske Anatomi, og Aetiologi. 1897.

serum and leukocytes infiltrating the lymph-spaces and to slight ruffling of the connective surface, just as grinding the surface of glass renders it milky. (*b*) Boggyness or edema of the valve is discernible at this time, due to the infiltration of the valve tissue as previously indicated. In this softened

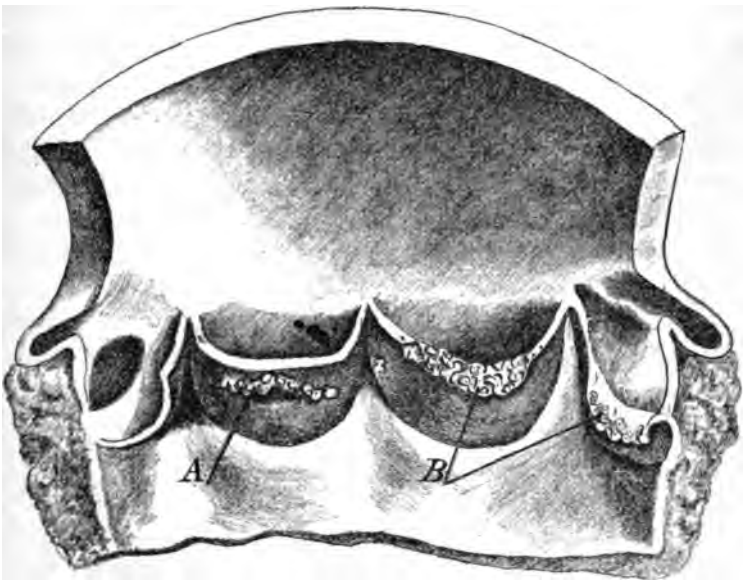

FIG. 230.—AORTIC ORIFICE LAID OPEN SHOWING THE VALVE LEAFLETS, ACUTE ENDOCARDITIS.—(*Redrawn from Schmaus.*)

A. Line of contact with beginning formation of vegetations. *B*. More advanced and larger vegetations closely simulating in appearance an ulcerative lesion. Between the leaflet *A* and the leaflet immediately above the letter *B* is seen a single vegetation on the leaflet *B*; should a similar lesion occur at the corresponding point on the leaflet *A*, the two coming together would afford a condition favorable to the development of an adhesion, which, after organization, might produce an adhesion between the two leaflets, thereby narrowing the orifice.

and boggy condition, the valves pounding against one another at the rate of 120 to 150 times a minute, (*c*) abrasion or even laceration may occur; the line of friction is the line of contact, and in this line roughened points develop.

Second stage: (*a*) The blood passing over the roughened

line of abrasion has fibrin whipped out upon the rough points; to this is added proliferation of some of the connective-tissue elements and of the leukocytes in the valve. These being most abundant at the focal point, increase the size of the so-called vegetation or cap of fibrin. With firm vegetations of moderate size, the lesion is called **endocarditis verrucosa**; when the collection of fibrin is large and flabby, the term **polypous** or **villous endocarditis** is at times applied. (*b*) Changes occur in the fibrin cap or vegetation; it may increase by layers (laminated); it may be re-dissolved; it may soften from being too large to organize; if near a corresponding mass on an opposite leaflet, especially at the valvular attachment, cohesion may occur; organization of the mass is the last process, and by some is considered as a third stage. Unless the process be fulminatingly rapid organization has begun, at the point of attachment to the valve, by the time it is visible to the unaided eye; as organization occurs, new blood-vessels may develop from the base of the valve.

FIG. 231.—ACUTE ENDOCARDITIS OF THE MITRAL VALVE, SECTION AT LINE OF CONTACT. (PARTLY DIAGRAMMATIC.)—(*Rindfleisch.*) × 10 diameters.

a, *a*. Endocardium which at *c* has become swollen and abraded and covered by the cap of fibrin, *d*. *b*. Interstitial tissue of the valve with newly-formed blood-vessels.

Results.—(1) Early the thickening or swelling muffles the valves and alters their sound. (2) Fenestrations may occur if not prevented by the cap of fibrin. (3) Laceration of valve leaflet, a further process than fenestration. (4) Adhesions of valve leaflets. (5) Induration, as organization occurs. (6) Contraction of the valve. (7) Calcareous or atheromatous changes. (8) Dilatation of the valve or orifice may occur early, from the softening and edema of the initial stage, or it may follow the atheroma. (9) A single valve leaflet may relax, producing what is sometimes termed *aneurysm of the valve.*

Acute Malignant Endocarditis.—(Synonyms, *Ulcerative*, *Mycotic*, *Bacteric*, *Pustular*, *Arterial Pyemia*, *L'Endocardite Vegetante Ulcereuse*, *Endocarditis Pyæmica*, *Diphtheric Endocarditis*, etc.)

Causes.—(1) Simple, may become malignant, and the chronic valve lesions are believed to predispose to this form. Goodhart found that 61 of 69 cases had been preceded by chronic endocarditis; (2) croupous pneumonia is the most frequent cause; in Osler's collection of cases, 54 out of 209 cases developed during an attack of croupous pneumonia; (3) erysipelas; (4) septicemia and pyemia; (5) osteomyelitis, probably due to this condition being commonly accompanied by septicemia or pyemia; (6) puerperal fever; (7) gonorrhea; (8) enteritis; (9) rarely, tuberculosis, typhoid, diphtheria, rheumatism, or chorea. The bacteria present: Streptococcus pyogenes; Micrococcus pyogenes aureus, also albus, cereus albus, and cereus flavus; the Diplococcus pneumoniæ, Bacillus fœtidus, and the alleged Micrococcus endocarditidis are believed by some to cause the disease. It seems probable that some injury or lesion of the value is necessary for implantation. (See alleged microbic causes of acute simple endocarditis on page 416.)

Site.—(1) Contact line of valves; (2) at base of valves; (3) mural; (4) interstitial in heart wall, presumed to be due to infective embolism of the coronary artery. As to orifice, Osler, Sansom, and Hamilton accept the following order: (1) Mitral; (2) aortic; (3) aortic and mitral; (4) heart wall; (5) tricuspid; (6) pulmonary. Guiteras believes the aortic orifice to be the most common seat.

Morbid Anatomy.—Whether preceded by a simple inflammation or not, ulceration and loss of tissue follow the infection; fibrinous caps may form over the ulcer, only to be swept off and become infective emboli; thickened deposit may occur around the ulcer; the valve may be disintegrated, or the car-

diac wall excavated or even perforated. Bacteria abound in the fibrinous caps and in the indurated base and edges.

Results—more or less destruction of tissue, infected embolic and disseminated infarction processes throughout the organism. Rarely, if ever, the patient recovers; if so, cicatrization and deformity of the affected area results.

Chronic Endocarditis.—(Synonyms, *Indurative*, *Sclerotic*, *Adhesive*, *Interstitial*, or *Permanent Endocarditis.*)

Causes.—(1) The result of the acute forms; (2) alcohol; (3) syphilis; (4) gout; (5) excessive work for any one valve, rarely all the valves, usually only those of the left side.

FIG. 232.—ADHERENT AND THICKENED VALVE LEAFLETS.—(*Rindfleisch.*)

View obtained by looking downward upon the aortic valves from the aorta. Two leaflets are adherent, all are contracted, thickened, everted, and unable to open widely or close tightly.

The results of acute endocarditis have already been described. Interstitial fibroid change developing slowly, showing as a milky opacity first at the margin of the leaflet, gradually extending, increasing the thickness and lessening the pliability of the valve, sooner or later contracting, undergoing calcareous change, etc. As contraction ensues, curling of the valve edges, insufficiency, and stenosis may develop. In figure 230 the valve leaflet on the extreme right is beginning to show slight eversion. The chordæ tendineæ thicken, agglutinate, or shorten so that the muscle may be apparently inserted immediately into the valve cusp; narrowing and adhesion leading to such conditions—for example, as the button-hole mitral. As the sclerosis advances, calcification may develop, and eventually the valves and orifices become hard, calcareous, fibroid masses, with hardly a normal element remaining. The mural form of chronic endocarditis is secondary to atheroma, or interstitial myocarditis, and shows merely as hard, fibroid, or calcareous areas on the cardiac wall.

Results of Endocarditis.—Where the valve does not

return to the normal, which in rare cases may occur, the changes already described lead inevitably to one of two conditions or to both.

(1) *Narrowing, Obstruction, or Stenosis.*—(*a*) Vegetations projecting into the lumen when the valve is open ; (*b*) stiffened valves which do not open ; (*c*) contracted valves which can not open, but subtend the orifice like a cord ; (*d*) adherent valves, the adhesions preventing opening ; (*e*) eversion or inversion of a leaflet either as a part or a whole ; (*f*) a lacerated leaflet hanging in the current ; (*g*) contraction of the orifice incident to a circumferential inflammation at the base of the valve, or, in the mitral, the free margin ; (*h*) loss of elasticity of the orifice due to fibrous or calcareous change, or to both, without of necessity contracting, but being inelastic it is practically a stenosis ; (*i*) combinations of these processes.

(2) *Insufficiency* or *incompetency* of the valves, permitting *regurgitation.*

(*a*) Valves may be propped open by a vegetation ; (*b*) valves may be too stiff to close ; (*c*) contracted valves can not close for the same reason that they can not open ; (*d*) inverted, everted, or lacerated valves can not close the orifice ; (*e*) fenestra below the line of contact permit regurgitation ; (*f*) contraction of the orifice leading to wrinkling of the leaflets is by some supposed to be a cause ; (*g*) relaxation, distention, or dilatation of the orifice beyond a size which the valve will cover or close.

It matters not which of the above processes occurs, the inevitable consequence will be increased work for the heart, and this must lead to either hypertrophy or dilatation.

HYPERTROPHY AND DILATATION.

Hypertrophy—	*Dilatation*—
Simple.	[Simple.]
[Eccentric.]	With thickening.
[Concentric.]	With thinning.

Simple hypertrophy is increased weight with increased functional power, without evident alteration in the cavity.

Eccentric hypertrophy is assumed to be increased weight, with increased functional power and increased cavity; in other words, it is the same as *dilatation with thickening;* during life the symptoms, if any presented themselves, were those of dilatation rather than hypertrophy.

Concentric hypertrophy is assumed to be hypertrophy at the expense of the cavity; that is, increased weight, etc., with diminution in the size of the cavity. It is a postmortem change, or is dependent upon the conditions which determine death. How easily one may be misled is illustrated by the following experiment:

Obtain three bullocks' hearts immediately on slaughtering, if possible. In one heart have all the vessels ligated before the animal is bled or the vascular system opened; let the second heart remain empty. The third heart is to be distended by ligating the pulmonary veins and attaching the aorta to a hydrant. It is best that all the hearts have about the same weight. In a few hours, when rigor mortis has ceased to act, the following will be found: The first heart is an example of hypertrophy with a normal cavity; the second, hypertrophy with diminished cavity; the third, hypertrophy with increased cavity. As death may arrest the heart in any degree of distention, or rigor mortis act to any degree, the above conditions may all be found in any hypertrophied heart. Simple hypertrophy therefore remains.

Dilatation with thickening is admitted, as is **dilatation with thinning,** but *simple dilatation* implies a larger cavity, with wall of normal thickness, and as this must weigh more, it requiring more muscle to surround a large cavity with a wall of a given thickness than a smaller cavity, as the normal, it is dilatation with increased weight, or thickening.

Causes of Hypertrophy and Dilatation.—Increased work

with abundant nutrition is followed by hypertrophy. Overwork, that is, work beyond the nutrition and muscular power of the organ, leads to dilatation.

These may be due to conditions *intracardiac* or *extracardiac.*

Intracardiac Causes.—(1) Any of the valvular lesions already given which increase the cardiac work. (2) Myocardial sclerosis. (3) Overstimulation of the cardiac muscle, as in alcohol, tea, and tobacco habituates.

Extracardiac Causes.—(1) The various forms of chronic pericarditis, adhesive, caseous, etc. (2) Diminished caliber of the vessels transmitting the blood—*e. g.*, narrowing or hypoplasia of the aorta, contraction of the arterioles, as occurs in Bright's disease. When the blood-vessels lose their elasticity from any cause the work of the heart is increased. (3) Increased muscular work demanding extra supply of blood, as in laborers and athletes. Hypertrophy is a physiologic process in gestation.

Hypertrophy of the left ventricle is by far the most common, but hypertrophy of the right occurs not infrequently. Those of the preceding causes, which may here act, are apparent, and to those may be added: (1) Backing of blood due to mitral disease; (2) narrowing of the pulmonary blood-vessels, as in congenital stenosis of the pulmonary artery. Emphysema, interstitial pneumonia, etc.; (3) valvular lesions of the right side; (4) tumors pressing upon the pulmonary artery.

Morbid Anatomy of Hypertrophy.—The apex is broadened, the wall implicated forms the apex, the conic shape is lost, the muscle is red and firm, cutting with more than the normal resistance. The test is increased weight; hearts weighing over 50 ounces have been reported. Reference has already been made to the unreliability of measuring the cardiac wall. Histologically, there is probably a numerical increase of muscle-fibers.

Life History of Hypertrophy. — Hypertrophy is not a disease, but a definite physiologic process with the distinct object of meeting a demand for more cardiac force : just as any muscle responds to an increased demand for power, the heart may respond. It is, however, imperatively necessary that the demand be not too suddenly developed, and that abundant nutrition be supplied to attain the desired end. It will be noticed that most of the causes above given are progressive in character and permanent in action, and will, therefore, indefinitely increase the demand for work ; or advancing years, with the concomitant changes in general nutrition, or the inroad of other diseases, such as Bright's disease, will reduce the body nourishment and lessen the available supply for the heart. In either case the compensation which nature has attempted may be overthrown by the wasting which the new changes will induce. Hypertrophy then passes into dilatation.

Acute dilatation, or *dilatation not preceded by hypertrophy*, undoubtedly occurs, and merely shows that the initial nutrition can not supply the initial demand ; ordinarily, this is met by the "reserve force" of the organ, but this may be deficient, as the result of general malnutrition or local disease, as occurs in granular degeneration and myocarditis, or the work suddenly thrown on the heart may be beyond the power of the reserve force ; in either case, the inability of the organ to fully perform its function, leads to accumulation of blood within the cavity and dilatation results.

Chronic dilatation usually follows hypertrophy, as above indicated, when compensation can no longer be maintained.

Morbid Anatomy of Dilatation.—Most common on the right side, and most marked in all the cavities in aortic incompetency. The auricles never hypertrophy without dilatation, and may attain enormous size. Dilatation of a cavity leads to dilatation of the orifices which communicate with it, and hence to incompetency. Opacity of the endocardium has been noted.

Microscopically, the muscle tissues may or may not show granular or fatty changes. Degeneration of the cardiac ganglia has been observed.

Influence of Cardiac Inefficiency on other Organs.—*Lungs*—Edema, congestion, brown induration, pulmonary apoplexy, bronchitis, croupous pneumonia.

Liver—Congestion, red or cyanotic atrophy, occasionally fatty.

Kidney—Cyanotic induration, infarctions.

Spleen—Congestion; the organ may be black or scarlet; indurated; infarction not uncommon.

Mucous membranes of the stomach and intestine—edematous; punctiform hemorrhages; sometimes fatty or atrophied.

BLOOD-VESSELS.

ARTERIES.

Normal Structure of an Artery.—(1) *Tunica adventitia*, or areolar sheath of fibrous tissue. (2) *Tunica media*; (*a*) in the larger blood-vessels this is mostly of elastic tissue with but little muscular fiber; (*b*) in the arterioles, the muscular fiber predominates and but little of the elastic tissue is present. (3) *Tunica intima* is histologically identical with the endocardium, and is known as the endangium; it lines the interior of all the blood-vessels and constitutes the wall of the capillary.

(I) **Atheromatous Arteritis.**—(Synonyms, *Endarteritis Chronica Nodosa s. Deformans.*)

Causes.—(1) Kidney disease; (2) old age, men more commonly than women; (3) syphilis; (4) gout and rheumatism.

Sites.—(1) Arch of aorta; (2) thoracic and abdominal aorta; (3) iliac arteries; (4) cerebral arteries, especially at the base; (5) rarely, arteries of the limbs; (6) rarely, the pulmonary artery; (7) in almost any of the large arterial trunks, particularly around the exit point of smaller branches

given off; thus, in the aorta the exit points of the coronary arteries and each intercostal branch may be surrounded by a rim of atheroma.

Morbid Anatomy.—(1) Milky opacity of the tunica intima; never universal, but confined to patches here and there; (2) elevation of these patches, due to thickening, cellular infiltration; (3) fatty areas in the patch, showing as a pale yellow spot, in the center of the patch, which spreads throughout the entire area; (4) deformity of the vessel, such as button-like elevations, usually most marked where a branch is given off; (5) changes in the spot, ulceration or calcification. These processes may all go on in the same vessel.

Morbid Histology.—Excess of fibrous tissue without blood-vessels, hence the tissue tends to become fatty. The degeneration commences near the media. The new tissue disintegrates, forming a small cavity filled with granular debris, oil globules, and occasionally cholesterin. Degeneration may spread to and invade the media; the intima may give way, causing an atheromatous ulcer.

Effect.—Loss of elasticity, weakening of the wall, and increased liability to aneurysm. The arterial tube being made rigid, increases the cardiac work. Where the process develops around the exit of branches,—as, for example, the coronary artery,—it may lessen the carrying capacity of the branch.

(II) **Arteritis Obliterans.**

Causes.—(1) Tertiary syphilis; (2) contracting kidney; (3) tubercular lung; (4) physiologic processes in the vessels of the fetus which become useless at birth, and in the arterial supply to the parturient uterus; (5) complete or partial occlusion of the vascular lumen.

Site.—Usually arteries of the brain.

Morbid Anatomy.—(1) Universal cord-like hardness; (2) lumen barely discernible, or the vessel may be closed. Outline of the vessel, as a rule, uniform, but may have annular

or nodular thickenings. There are none of the yellow patches of the atheromatous variety. Baumgarten regards the annular and nodular thickening as perivascular gummata.

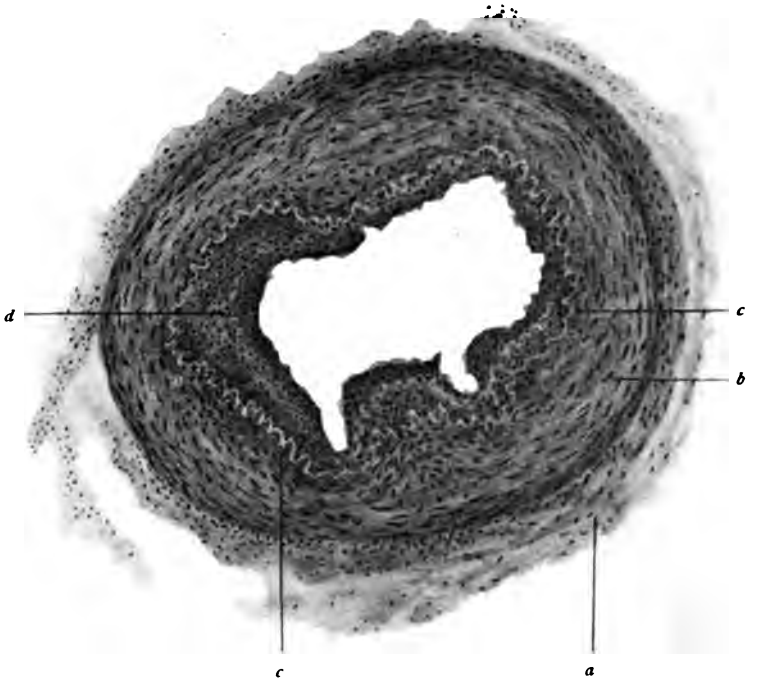

FIG. 233.—OBLITERATIVE ENDARTERITIS.—(*The original, from which drawing was made, was removed from near a cancer of the face, and prepared in the laboratory of the Jefferson Medical College Hospital by Dr. Thomas Leidy Rhoads.*) 1-inch objective, 1-inch ocular.

Specimen fixed in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. *a*. Adventitia. *b*. Media. *c, c*. Elastic lamina. *d*. Irregularly thickened intima. The gross specimen was hard, cord-like, but not nodular.

Morbid Histology.—(1) Intima becomes milky, as in the atheromatous, but does not become fatty; (2) the sclerosed areas are uniform; (3) thickened intima encroaches on the lumen; (4) young blood-vessels develop to supply the new tissue; hence

no fatty degeneration. Differs from the atheromatous in that (*a*) it is a disease of small arteries, not large ones; (*b*) thickening is circumferential; (*c*) thickening becomes vascular and not fatty; (*d*) obliterates and does not favor aneurysm; (*e*) other signs of syphilis or some chronic infection are not uncommonly present.

Effects.—(1) Cuts off blood supply to tissues. In the brain, softening and paralysis ensue; neuralgia, if the root of the fifth nerve be implicated. (2) In the fetus, destruction of an organ, as the kidney, results from cutting off the blood supply during development. (3) Prevents hemorrhage, as in tubercular and other ulcerative processes.

(III) **Arteritis Infectiosa.**—Includes the *suppurative*, *malignant*, or *ulcerative* inflammation of the arteries. It may be (*a*) *mural* and (*b*) *interstitial*.

Causes.—Introduction of pathogenic bacteria into a blood-vessel—*e. g.*, from wounds, peri-arterial infection, septic thrombi, septicemia, etc.

The *mural* variety is due to the direct implantation of bacteria on the surface of the intima; the changes which ensue are analogous to those of malignant endocarditis. The implantation may be primary or secondary.

The *interstitial* form may follow injury with infection, or may occur as the result of a general infective process. It may follow the mural form. In some instances it probably represents infection by the vasa vasorum. Inflammation, terminating in pus formation, occurs in the media or adventitia, or both. There is also proliferation of the cells of the intima, producing roughness, and this in turn leads to fibrin formation or deposit on the wall, and thereby engenders infective thrombi. The same process occurs in the veins—*e. g.*, infected uterus, infected cranial sinuses from mastoid disease.

(IV) **Endarteritis Verrucosa,** or *Warty Endarteritis.*—The condition is rare, and is probably the result of organ-

ized thrombi on the vessel wall; it is usually found in the larger vessels, aorta, iliac, or femoral arteries.

Morbid Anatomy.—Smooth warty growth on the interior of the vessel, the same color as the intima, and projecting into the lumen of the vessel.

Morbid Histology.—The mass is composed of young-cell elements made up, for the most part, of fibrous tissue cells.

(V) **Periarteritis Simplex** (*Charcot*).—This condition is non-suppurative, occurs in the vessels of the brain, and leads to miliary aneurysm. It first attacks the adventitia as a small cell infiltrate, which invades the media later, and the intima last, if at all. The softening weakens the vessel and leads to aneurysm. The disease is most common in the smaller arteries, but may invade the capillaries or the larger arteries of the base.

While the cause is not established, syphilis seems able to induce the change.

(VI) **Periarteritis Nodosa.**—This condition has been described as occurring in the vessels of the heart (coronary artery), stomach, kidney, spleen, and muscles. The vessels are at points dilated, and at other points contracted. Infiltration with a rich cellular deposit occurs in the outer coat of the vessel; the media becomes fatty, but the intima is not affected. The small sac-like dilatations not uncommonly contain clots.

(VII) When an inflammation involves an artery by extension from contiguous tissues, the process is spoken of as a **secondary arteritis**, and partakes of the essential features of the inflammatory process which caused it.

Arteriocapillary fibrosis or **arterial sclerosis** occurs in (1) contracted kidney, (2) cardiac hypertrophy without contraction of the kidney, and (3) in combinations of the two.

The change is one of increased fibrous and muscular tissue

in the wall of the arteriole. Gull and Sutton were inclined to believe that contracted kidneys were a part of a general process rather than that the general condition was secondary to the kidney lesion.

Calcification of blood-vessels occurs (1) as a result of atheromatous endarteritis or other inflammation of the vessel; (2) *cryptogenic calcification* is where lime salts are deposited in the vascular wall without any discernible antecedent disease.

Ossification, or true bone formation, is said, by Orth, to be a possibility; exactly what induces it, or how it may be brought about, is not known.

Hyaline, vitreous, or **diaphanous degeneration,** identical with that described by Zenker as occurring in the muscles, has been found in the vessel walls, usually in the arterioles.

Wax-like, albuminoid, or **amyloid infiltration** has been considered in connection with amyloid infiltration (see p. 111).

Fatty degeneration of the blood-vessels is a disease of the capillaries, small arteries, and, rarely, the veins. It occurs most commonly in the capillaries of the brain. As to cause, it occurs in connection with (1) old age, (2) pernicious anemia, (3) phosphorus poisoning, (4) general debilitating conditions.

The change in the intima resembles the degenerative lesion of atheroma, but is not accompanied by any fibrous-tissue formation or other phenomena so constantly associated with atheroma.

Histology.—The vessel walls are converted into fatty cellular debris without any preceding inflammatory process like that of atheroma.

An **aneurysm** is a tumor-like sac, containing blood and communicating with an artery.

The *sac* may be made up of one or more coats of the blood-vessel, when it is known as a *true aneurysm—arterial ectasia;*

where the sac is made up of the condensed tissues around the

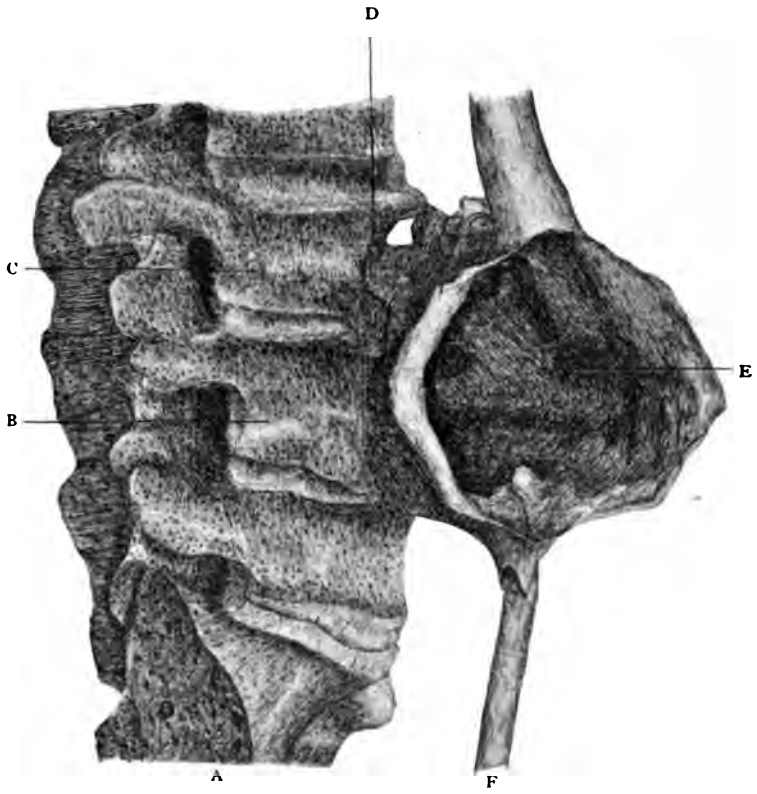

FIG. 234.—SYMMETRIC ANEURYSM OF THE ABDOMINAL AORTA.—(*Specimen in the museum of the Jefferson Medical College.*)

A. Sacrum. B Fourth lumbar vertebra; the anterior part of the body has been eroded by the aneurysm. The inferior margin has had thrown out calcareous material which, anteriorly, covers the cartilage. C. Body of third lumbar vertebra. At D the aneurysmal sac has been cut away to show the absorption of the body of the vertebra. E. Cavity of the aneurysm. At the lower part of the cavity, between the points of exit of the two iliac arteries, a sharp spicule of a calcareous plaque will be seen projecting upward. F. Left iliac artery; the right iliac artery will be seen as a short stump at the lower part of the aneurysmal wall.

vessel, the latter's walls having entirely given way, the condition is spoken of as a *false aneurysm.*

Causes of Aneurysm.—Aneurysms are said to be (1) *traumatic* or (2) *idiopathic.* As nothing occurs without a cause, it would be better to refer to the latter as *cryptogenic.* Further, the causes of aneurysm are said to be (1) *predisposing* and (2) *exciting.* Of the former, any of the degenerations of the arterial coat which we have just studied, and which weaken the artery, are eminently predisposing. Age: between the thirtieth and fortieth years of life the arterial changes described in the preceding pages are likely to first evince themselves; the heart is yet in full power, in most individuals, and, with the maintained cardiac force and diminished strength of the diseased arterial wall, rupture or dilatation of the blood-vessel is likely to ensue. Suddenly developed, powerful cardiac force such as may occur from a hard lift, sudden spring, or vault, doubles the demand on the semirigid and weakened vessel walls. The male is more liable to these sudden exertions, and hence aneurysm is much more prevalent in that sex. Injury to the blood-vessel may be an exciting cause or a predisposing element; if the injury be a puncture, it may be followed, immediately, by a false aneurysm; if a contusion, the arterial changes may be such as to weaken the wall so that it gives way upon a slight strain in the future. Stretching and twisting of vessels, as in dislocations and fractures, or in their reduction, has been followed immediately by aneurysmal dilatation.

Form of Aneurysm:

(A) *Classified by the shape:* (1) *Cylindric*, uniform distention of the vessel; (2) *fusiform*, or spindle-shape; (3) *cirsoid*, a number of arteries irregularly dilated; where a single artery is involved, the term *aneurysmal varix* is used; (4) *saccular*, in which a distinct pouch is formed; if on one side of the vessel and communicating by a small opening, it is spoken of as *asymmetric;* if the sac be uniformly distributed around the vessel, as in the miliary aneurysm of the brain, it is *symmetric;*

(5) *arteriovenous aneurysm*, where injury has established communication between an artery and a vein; (6) when the wall sharply defines the aneurysm, it is spoken of as *circumscribed;* when the blood cavity terminates in infiltrated tissue, the term *diffused* is applied.

(B) *Classified by the cause:* (1) *Traumatic*—an aneurysm arising suddenly as from an ulcerative endarteritis or trauma is sometimes spoken of as an *acute aneurysm;* (2) *idiopathic* or *cryptogenic;* (3) *embolic*, due to proximal distention in occluded vessels, usually terminal; (4) *dissecting aneurysm* due to blood dissecting between the layers or coats of a vessel's wall; (5) *verminous aneurysm*, one containing a parasite such as is found in the mesentery of the horse (Osler).

(C) *Classification based on duration and changes in the wall:* (1) An *acute aneurysm* or *recent aneurysm* is one quickly developed and usually traumatic; (2) *chronic* or *old aneurysm*, an aneurysm which has persisted longer, as shown by the changes which its walls have undergone.

Results of Aneurysm.—(1) Disturbance of blood-distribution; (2) pressure on surrounding tissues and organs; (3) rupture; (4) cure and arrest of further circulation through the altered vessel.

Cure of Aneurysm.—(1) Clotting or fibrinous deposit must occur; this may be in layers (laminated), or it may be a central clot apparently formed as one mass. By occluding the point of exit the circulation is arrested; (2) the coagulum may remain unaltered for years. The writer saw a case in which all symptoms, except the presence of the tumor, had been absent for eight years, the proximal and distal ends of the vessel having undergone obliterative arteritis; (3) in time, blood-vessels may permeate the clot and organization of the mass ensue; (4) the young blood-vessels may dilate, canalization occur, and re-establish the circulation (see "Canaliza-

tion of a Thrombus," p. 147); (5) a mass of fibrous tissue may remain and mark the site of an aneurysm.

Hypertrophy of Arteries.—When a large arterial trunk is obstructed, the blood supply to the part beyond may be maintained by enlargement of branches, rising above the point of obstruction, and these anastomosing with branches from below, which may also increase in size. The condition is one apparently of true hypertrophy. The anastomotic circulation eventually becomes as competent to carry on the functions of nutrition as were the normal vessels. When this occurs, it is said that a collateral circulation has been established by anastomosis.

VEINS.

Normal Structure.—Veins have, normally, the same structure as arteries, except that the tunica media is very much less developed, and hence the walls are thinner. Many of the veins are supplied with valves and thus differ from the arteries.

Inflammation of Veins—Phlebitis.—Inflammatory processes analogous to those already described as occurring in the arteries take place in the veins, the most important of which are the infective forms—**infectious phlebitis.** As here the current is from the smaller lumen to a larger one, dislodgment occurs, and emboli are thrown off in large numbers. When considering thrombosis and embolism this point was mentioned. The source of the infection in veins may be by (1) direct infection, as in wounds; (2) mural implantation; (3) continuity of spread; that is, passing directly along the vessel wall; (4) by contiguity. As examples of the last two, we have spread from infected uterine sinuses to pelvic veins, and spread from mastoid disease to the brain sinuses respectively. Pyemia and other systemic septic conditions may result.

Varicose Veins, or Phlebectasia (Synonyms, *Varix*, *Varicosity*).—This condition consists of more or less irregular

dilatation of the veins, as a rule, associated with alterations in their walls and nutritive changes in the area involved.

Sites.—Veins of the leg and veins of thigh; plexus pampiniformis; hemorrhoidal veins; occasionally the veins of the abdominal wall, and rarely intra-abdominal veins, peri-uterine, nephritic, or mesenteric.

FIG. 235.—VARICOSE VEINS OF THE LEG.—(*Gould.*)

Causes.—(1) Obstruction to the onward flow of the blood—*e. g.*, tumors of the pelvis, pregnancy, etc., inducing varicosity of the veins of the leg and of the rectum; cirrhosis of the liver, obstructing the veins returning from the alimentary canal; tight garters are also a cause; (2) diseases of the central organ of circulation, leading to venous stasis; (3) pulmonary obstruction leading to backing of the blood into the veins; (4) inflammation of the veins, (*a*) leading to softening of the walls, and thus favoring expansion, and (*b*) obliterating or narrowing a large vein, such as the femoral, by a thrombus, or by contraction, and thereby increasing the intravenous pressure in the vein beyond the point of obstruction.

Forms.—(1) Where the dilatation is regular, symmetric, and not associated with lengthening, the dilatation is spoken of as *simple;* (2) when the vein is dilated and tortuous, due to apparent lengthening as well as dilatation, it is spoken of as *cirsoid dilatation;* (3) where the dilatation is irregular, saccular, or upon alternate sides, the condition is spoken of as *varicose dilatation.*

Results of Phlebectasia.—The slowed circulation, passive congestion, lessens the nutrition in the tissues of the area drained by the vessels involved, by failure to remove effete materials; edema occurs; clots may form in the vein; the stretching of the walls renders the valves inefficient; as a

result of the lowered vitality, slight bruises or superficial excoriations are followed by infection in the diseased area, and extensive ulceration ensues. In the testicle, lessened nutrition undoubtedly results, and in some instances this may be followed by atrophy of the organ. In the rectum, clotting may occur in the dilated hemorrhoidal veins and violent inflammatory processes follow, or the venous mass may ulcerate and bleed, or may, by its size, cause more or less obstruction to the passage of fecal matter.

Tumors of Blood-vessels.—Primary tumors of the blood-vessels are rare. They must be of the connective-tissue series. Sarcomata invade the vessels rapidly and particularly the veins, by which they not uncommonly spread. The cancers can implicate the vessels only as secondary growths, and this they rarely do. (For tumors of the blood-vessels, blood-vessel tumors, see "Angiomata," p. 198.)

Tuberculosis of blood-vessels occurs as a mural implantation of the bacilli, or by invasion of the blood-vessel wall by a tubercular process from an adjacent tissue.

Syphilis of the vascular system has been considered under each condition in which it may occur.

QUESTIONS.

(1) What are the malpositions of the heart? (2) What is it called when on the right side? (3) If right-sided, with what else is it likely to be associated? (4) What do you mean by the situs inversus? (5) What are the other malpositions of the heart? (6) If the heart is below the diaphragm, what is it called? (7) What is meant by (*a*) pectoral heart, (*b*) cervical heart, (*c*) ectopic heart? (8) What are the ordinary malformations of the heart? How are they divided? (9) How may the heart be malformed? What arrest in its development may occur? (10) What malformation of the septum do you most commonly find? (11) What perforate septum is most frequently retained during adult life? (12) What are the degenerative changes which may occur in the heart? (13) What form of degeneration is cloudy swelling? (14) What are the

forms of fatty degeneration? (15) What are their essential differences? (16) What do we mean by local fatty degeneration, and what is its cause? (17) What are the causes of general fatty degeneration? (18) What are the forms of atrophy of the heart? (19) What is the cause of local atrophy of the heart? (20) Where does it usually manifest itself? What part of the heart? (21) What conditions may give rise to almost no blood getting into the left ventricle? (22) What valve? (23) What is the cause of general atrophy of the heart? (24) In what conditions would you expect to find general atrophy of the heart? (25) In what diseases? (26) Under what condition are you likely to have aneurysm of the heart? (27) From what kind of fatty degeneration of the heart? (28) What other causes of aneurysm may you have? (29) What form of inflammation of the heart muscle is likely to develop aneurysm? (30) In what diseases of the blood are you likely to have local inflammation of the heart muscle? (31) Of what structures are the walls of a cardiac aneurysm composed? (32) Suppose you have an area of inflammation in the cardiac wall, the case gets well, and comes to the postmortem table years later, what evidence would you have of the existence of the former inflammation? (33) Where are the inflammations and aneurysms and areas of local degenerations most commonly located? (34) What part of the left ventricle is most likely to be involved? (35) How would you differentiate antemortem from postmortem clots? (36) How are you going to tell how old the clot is—whether it occurred just before death, or whether it is considerably older? (37) What is the normal structure of the endocardium? (38) What structure in the blood-vessels is analogous to the endocardium? (39) Which side of the heart has the most work to do? (40) Where is inflammation of the endocardium most likely to occur? (41) What malformations of valves may you have? (42) What are the local manifestations of acute inflammation of the valve? (43) Why do they abrade themselves? (44) Where is the line of abrasion, or laceration, should it occur? (45) Following this, what changes take place on the valve? (46) What change may this cap of fibrin undergo? (47) What is the difference between this acute simple inflammation and the malignant? (48) Where may this process occur except in the valve itself? (49) What is the cause of ulcerative endocarditis? (50) Is it necessary that the valve be inflamed before the bacteria attack it? (51) In what diseases does endocarditis occur? (52) What classes of fevers may be accompanied by it? (53) Is there any germ which specifically induces endocarditis? (54) Are the microorganisms of suppuration able to produce this change? (55) Under what conditions are the organisms of suppuration found in the blood? (56) What conditions are likely to accompany or arise as a result of ul-

cerative endocarditis? (57) What is the character of the emboli? (58) What else may break down besides the vegetation? (59) Besides upon the valve leaflet, is there any other form of ulcerative endocarditis? (60) When it does occur on the walls, by what is it accompanied? (61) What weakens the wall? (62) What are the causes of chronic endocardial inflammation? (63) What are the changes in the valve of chronic inflammation? (64) To what is the thickening in chronic inflammation due? (65) Does chronic endocardial inflammation occur anywhere else than on the valves? (66) When it occurs on the walls what is it called? (67) With what is that usually associated? (68) What changes occur in orifices and valves as a result of endocardial inflammation? (69) What is partial occlusion of orifices called? (70) What may give rise to the stenosis? (71) When a valve thickens, what does it do? Wherever young fibrous tissue occurs, what takes place? (72) What else may produce narrowing? (73) What conditions may give rise to insufficiency? (74) Dilatation of what? (75) What do you mean by fenestrated valves? (76) Under what conditions may a fenestrated valve not be competent? (77) All of these conditions have what influence upon the heart's work? (78) Whether it is hypertrophy or dilatation is dependent upon what? (79) What are the forms of cardiac hypertrophy? (80) Take a heart with simple hypertrophy: under what conditions might you be led to infer that it is either eccentric or concentric hypertrophy? (81) What are the forms of dilatation? (82) How does the cause of dilatation differ from hypertrophy? (83) Why does dilatation follow hypertrophy? (84) Which ventricle is most commonly involved in hypertrophy? (85) Which one in dilatation? (86) How may diseases of the left heart induce diseases of the right heart? (87) Give causes of hypertrophy? (88) What causes are cardiac? (89) What extracardiac? (90) What causes may induce the change in the right heart? (91) What is acute dilatation? (92) Describe a dilated heart. (93) What influence may cardiac inefficiency have upon the lungs? (94) Upon the liver? (95) Upon the spleen? (96) Upon the kidney? (97) Upon the mucous membranes of the alimentary canal? (98) What is cardiac dropsy? (99) To what is it due? (100) What is the normal structure of (*a*) an artery, (*b*) a vein, (*c*) an arteriole, (*d*) a capillary? (101) Give causes, distribution, and effect upon the blood-vessel of atheromatous arteritis. (102) Give same for arteritis obliterans, and how does it differ from the atheromatous arteritis? (103) Give the forms of infectious arteritis, and mention an example of each form. (104) How does periarteritis simplex differ from infectious arteritis? (105) What is warty endarteritis? (106) Give morbid histology of arterial sclerosis, and mention diseases with which it is most commonly associated. (107) What degenerations

occur in the blood-vessels? (108) What is an aneurysm, and what are its causes? (109) Give the forms of aneurysm, classified by shape. (110) What is meant by traumatic aneurysm? (111) Dissecting aneurysm? (112) Under what condition is an aneurysm said to be (*a*) circumscribed, (*b*) diffuse? (113) How may any aneurysm be obliterated by natural processes? (114) Under what conditions may a true vascular hypertrophy occur? (115) What are the forms of phlebitis? (116) Give forms of septic phlebitis and mention an example of each form. (117) What is varicocele? (118) What is an internal hemorrhoid? (119) What are the causes of phlebectasia? (120) What are its forms and results? (121) What tumors are most likely to spread by the blood-vessels? (122) How may tuberculosis occur in the vascular system?

CHAPTER IV.

MUCOUS MEMBRANES.

Normal Structure.—A mucous membrane consists essentially of three parts: (1) Upon the surface, a layer of epithelial cells; (2) a basement membrane upon which these cells rest; (3) the submucous connective tissue, in which ramify the blood-vessels, lymphatics, and nerves essential to the life and functions of the layers above.

(1) *The epithelial layer* varies in two particulars, (*a*) the character of the epithelium and (*b*) the number of layers. Where the function of the epithelium is protective in character it is found in a number of layers; where secretion is the essential function there is commonly but one layer—*e. g.*, on the tongue numerous layers are found, while in the tubules of the stomach, the acini of glands, and the tubules of the kidney, etc., but a single layer exists. Where, in addition to protection, propulsive force is needed, or where the latter alone is demanded, the epithelial cells are supplied with cilia, as in the bronchi, Fallopian tubes, etc.

Epithelial cells possess the remarkable faculty of manufacturing, from supplied nutrition, new chemic compounds not existing, as such, in the pabulum supplied—*e. g.*, the secretions of the salivary glands, the gastric follicles, the pancreas, kidney, etc. Every mucous surface is therefore a laboratory, and this peculiarity has given the membrane the name specialized, indicating that it possesses characteristics eminently its own. While all mucous membranes elaborate something, the most constant element is mucus; when altered by disease, it not uncommonly is the sole product of a tissue

whose function is the manufacture of a material to be further utilized by the economy, or the excretion of an agent for which the organism has no further use, and when such perversion of cell activity exists, the evidences are not slow to appear. As the function of the cell is dependent largely upon the pabulum supplied, and as this supply is controlled by the subepithelial layers, it becomes evident that alteration of the basement membrane or the submucosa must affect the activity of the superimposed epithelium.

(2) *The basement membrane* (membrana propria) is composed essentially of two layers, one of which is always present; the other may or may not be demonstrable. The outer layer is composed of that part of the epithelium which reproduces the cells above, and is the genetic layer; it may or may not be demonstrable, and is, possibly, absent in a few membranes; such surfaces, if deprived of their epithelium, recoat from the margins exactly as an ulcer would do. The essential layer of the basement membrane which is always present is the connective-tissue layer. This is composed of fibrous tissue and, in some situations, a scant supply of unstriped muscle cells. The thickness of the basement membrane varies greatly; thus in the mouth and nose it is of a discernible thickness, while in the pulmonary alveoli it is demonstrated with difficulty. Where great changes in the volume and surface of the organ are likely to occur, the basement membrane may be thrown up in irregular ridges. By some it is claimed that the nerves and lymphatics penetrate this structure and present themselves immediately in the epithelial layer. It is not, however, probable that such is the case; the basement membrane being the line between the connective and epithelial tissue, it seems extremely probable that it is merely pushed as a thin layer ahead of the nerve-fibers, and that the lymphatics open by stomata immediately beneath or into the genetic epithelial layer of epithelium when such exists.

(3) *The submucosa*, or submucous connective-tissue layer, is of the greatest importance, and varies more than either of the preceding. In a part of the nasal fossæ it is erectile; where an organ is subject to great alteration in surface, like the stomach, it is especially abundant; where it is not to be called upon for such alterations in surface at such rapid intervals, it may be wanting, as in the uterus, where it is extremely scanty if present at all. As the nutrition of the epithelium is largely dependent upon the condition of the submucosa, lesions of this layer influence the function and structure of the overlying mucosa.

DISEASES OF THE MUCOUS MEMBRANES.

Hyperemia may be a physiologic process, as in the increased blood supply sent to the digestive organs when digestion is in progress. (For "Pathologic Hyperemia" see "Inflammation.")

Congestion of a mucous surface is dependent upon conditions which interfere with the return or exit of the blood. Congestion is seen in the lungs and upper air-passages and in the alimentary canal, as a result of cardiac disease associated with interference in the onward flow of the blood, and in the stomach and intestinal mucous membranes in obstructive hepatic disease as well. It may or may not be the precursor of inflammation, and its permanency is dependent upon the condition which causes it.

The function of the membrane is materially altered by the faulty metabolism which always attends a stagnant circulation. In time an increase in the fibrous tissue of the submucosa occurs, usually preceded, accompanied, and followed by a catarrhal process manifested in the epithelial layers above. In obstructive diseases of the lungs or heart, the congestion of the gastric mucous membrane may be so great as to resemble poisoning.

Hemorrhage from the mucous membrane occurs as a physiologic process in menstruation; hyperemia and congestion not uncommonly terminate in hemorrhage, as in yellow fever, congestive malaria, and allied conditions. It is not always an evidence of any serious malady, as is shown by trifling epistaxis without apparent cause. In hemophilia and scurvy, epistaxis is the common occurrence. As to severity, the hemorrhage may be the trifling escape of a few red corpuscles in an abundant mucous exudate (serosanguineous) or it may be alarming; the escaped blood may pour out on the surface as in epistaxis, or it may infiltrate the submucosa (interstitial or purpuric hemorrhage) and show postmortem in the intestines or elsewhere as purpuric spots. During life, in purpura, exposed or visible mucous surfaces may exhibit the discolorations in a typic manner. These spots, if large, may give rise to sloughing (gangrene) in very exceptional cases, and, if the patient survive, ulcers may develop, although this is rare; as a rule, if recovery occur, the blood is absorbed without any septic or gangrenous process.

Atrophy of the mucous membrane (see "Inflammation").

Hypertrophy of the mucous membrane (see "Inflammation").

INFILTRATIONS OF THE MUCOUS MEMBRANES.

Pigmentary Infiltration.—(A) **Pneumonokoniosis:** Solid particles may gain ingress to or through the mucous membrane from the surface, as in laborers whose occupation exposes them to the constant inhalation of suspended solid matters—*e. g.*, the inhalation of coal-dust by laborers in anthracite mines leads to a condition in the lungs known as **anthracosis**; in the grinders of metal instruments, in nailers, etc., iron inhaled leads to an allied condition known as **siderosis** (where the disease occurs in nailers it is also known as *nailer's phthisis*); in the makers of grindstones, stone-cutters, etc., the disease is known as **lithosis** or **chalicosis.** Similar infiltrations occur in laborers in cotton

and shoddy mills, and in the handlers of grain. These pigment particles do not seem to be able to penetrate the stratified epithelium, but gain ingress further down in the air-passages; the alveoli being permeable, the epithelial cells not arresting all the pigment; it enters the lymph-spaces of the basement membrane and from there diffuses by the lymphatic channels into the surrounding tissues. The deposited material finds lodgment in the following structures (Hamilton): subpleural and interbronchial tissues; in the peribronchial glands; in the lymphadenoid interspaces of the alveoli.

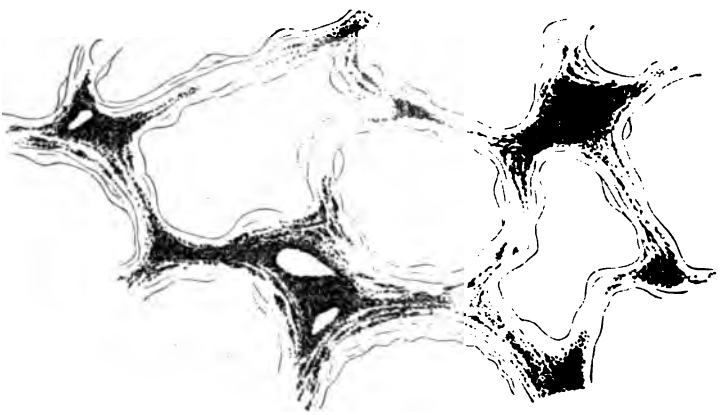

FIG. 236.—SECTION OF THE LUNG, PNEUMONOKONIOSIS.—(*Rindfleisch.*)
The deposited pigment is shown in the connective tissue of the vesicular wall.

After the disease is well advanced in the pulmonary tissues, the substernal and general mediastinal glands may be infiltrated. Weigert asserts that the circulation may be reached by the pigment passing through the peribronchial glands which attach themselves to the pulmonary veins into which they may rupture. The presence of foreign solid material induces inflammation of the mucous covering, at first acute, but from the continued application of the irritant the changes incident to chronic inflammation occur. In the deeper tissues fibroid

hyperplasia ensues, with the abundant production of new fibrous tissue in the infiltrated areas. The catarrhal processes denude the epithelial protecting layer, and the lung tissue becomes exposed to the dangers of infection by bacteria. Pyogenic organisms lead to infective inflammation and softening in the fibrous areas, and eventually to cavity formation;

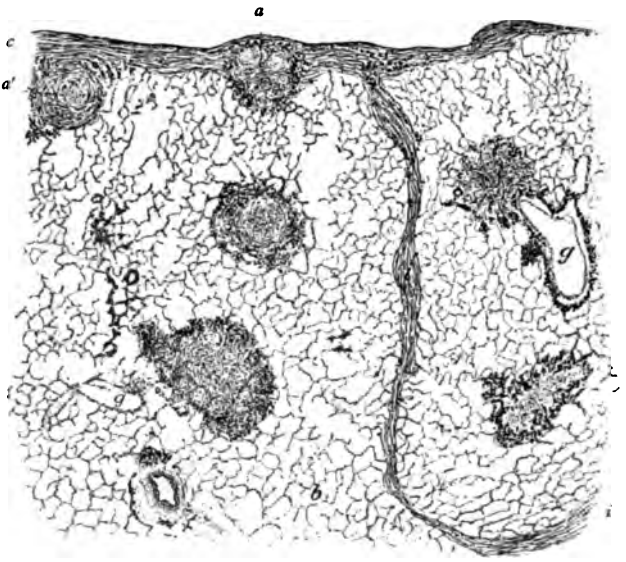

FIG. 237.—SECTION OF LUNG SHOWING CHALICOSIS.—(*Schmaus.*)

a. Collection of infiltrated material lodged in the pleura, *c*. A capsule of fibrous tissue has formed around it. *a'*. Similar nodule in the lung tissue. Other nodules are shown. *b*. Unaffected pulmonary tissue. *c*. Pleura. *g*. Blood-vessel, around one branch of which a nodule is forming. *i*, *i*. Interlobular septum, showing some thickening.

or, what is much more common in susceptible individuals, tubercular infection terminates the case. Aside from the lung a similar pigmentary infiltration is occasionally seen in the vomer and turbinated bones.

Occasionally metallic substances taken as medicines, or otherwise, may be precipitated in or on the mucous membranes

with which they come in contact. Examples of this are seen after the administration of iron or bismuth.

(B) **Pigment deposit from the blood. Brown induration** of the lung is in part a pigmentary infiltration, secondary to chronic congestion. The disease is most marked in the lung in chronic heart disease. The alveolar epithelium contains altered blood pigment, and pigmented cells are found in the interalveolar wall. The capillaries are distended and the fibrous tissue of the lung increased in amount. The lungs, on opening the chest, do not immediately retract; they are at first brownish-red in color, but on exposure to the air they become livid red from the oxidation of the excessive quantity of hemoglobin; the tissue is denser than normal, cutting and tearing with considerable resistance.

Deposition of coloring-matter is found in other mucous membranes, where constant or repeated congestions occur, as in malaria; the intestinal, gastric, and hepatic tissues showing the change in the highest degree.

Fatty infiltration seems exceedingly rare, if it ever occurs in a mucous surface. The writer has never seen it. In the glands of the mucosa it may occur, and in the liver is rather frequent (see "Fatty Infiltration of the Liver," p. 110).

Albuminoid or amyloid infiltration, when the general disease is present, invades the mucous membrane (submucous blood-vessels) of the stomach and intestines, rarely the gullet or the air-passages (see "Infiltration," p. 111).

Calcareous infiltration occurs as secondary to chronic inflammatory changes.

DEGENERATIONS OF THE MUCOUS MEMBRANES.

Granular degeneration, or *cloudy swelling*, occurs in the various epithelial structures as the result of high temperature, overwork, or beginning inflammatory change; it is seen to the best advantage in the epithelium of the kidney and liver.

Fatty degeneration, or *fatty metamorphosis*, representing, as it does, a later stage of the granular process, will be seen when the latter condition has lasted for any length of time with persistent or progressively increasing causes. It has been noted in pernicious anemia.

Coagulation necrosis is a composite degenerative process which occurs in mucous membranes under certain conditions. If the blood supply to an area be cut off the area dies, if collateral nutrition be insufficient. Exactly what the ultimate processes which go on in such an area are, is problematic.

FIG. 238.—GRANULAR DEGENERATION (CLOUDY SWELLING) OF THE LIVER CELLS. —(*Schmaus.*)

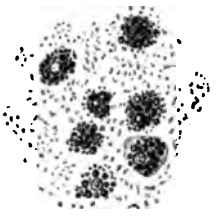

FIG. 239.—FATTY DEGENERATION OF THE LIVER CELLS.—(*Schmaus.*)

FIG. 240.—GRANULAR DEGENERATION OF THE KIDNEY EPITHELIUM (CLOUDY SWELLING).—(*Schmaus.*)

Fibrin will be found matting the elements together, and later granular, fatty, and infective changes lead to its absorption, separation, or ulceration ; the infective changes, if pyogenic, lead to ulceration or abscess formation, and occasionally, on mucous surfaces, a wide-spread lymphatic infection finds entrance through an area which has undergone coagulation necrosis—*e. g.*, streptococcus infection of the lymphatics, accompanying or following diphtheria. Coagulation necrosis most commonly follows infective processes as typhoid fever, diphtheria, etc., but may result from emboli lodging in the vascular supply of the submucosa, the infarcted area disappearing

by coagulation necrosis. By some, this is spoken of as a *hyaline* or *fibrinous transformation.*

Coagulation necrosis is by some classed as a degeneration, but as it occurs almost exclusively in consequence of inflammation, it is separately considered.

INFLAMMATION OF THE MUCOUS MEMBRANES.

There is probably no tissue in the body so prone to inflammatory processes as the mucous membranes, and as these inflammations occur as the result of many and complex causes, and are modified by the character of the membrane as well as its function and the cause, to describe each anatomic and etiologic form would require more time and space than is allotted to the present volume. For convenience of description the inflammations are divided into the (1) catarrhal, (2) pseudomembranous, (3) hemorrhagic, (4) gangrenous, (5) suppurative, (6) chronic infectious.

(1) **Catarrhal inflammations** are clinically spoken of as (*a*) *acute* and (*b*) *chronic;* pathologically, they occur as more or less acute processes, becoming chronic by prolongation of one stage of the acute, or, by repeated attacks, changes are induced which are, in many instances, permanent.

(*a*) **Acute catarrhal inflammation** arises as a result of many complex causes applied from without, or exerting their influence from the circulatory side of the membrane. Inflammations of the mucous membranes arise, most commonly, from some form of infection. Nearly all the acute infectious diseases, such as measles, scarlet fever, typhus fever, diphtheria, etc., are accompanied by, or may incite, a catarrhal inflammation of one or more mucous surfaces; the same is true of the chronic infectious diseases, such as tuberculosis and syphilis, if they occur in the mucous membrane.

The application of irritants to the mucous surface is, next to infection, the most common cause, and embraces a multitude of

sub-causes—*e. g.*, foreign bodies ; heat, as by hot air, steam, or a liquid such as hot water ; irritant gases, as chlorin, bromin, ammonia, sulphurous acid ; poisons, such as escharotics like the mineral acids, arsenic, etc., in dilutions too weak to actually destroy the surfaces with which they come in contact. Inflammatory conditions, in the mucosæ, may also arise from irritants due to chemic changes in foods, whether the irritant be preformed when the food is taken, or develop subsequently by fermentation or other change ; as examples of these we have the ptomain poisonings and the gastric catarrh due to fermenting food. Alcohol is also a cause.

While rapid thermal and barometric changes and excessive humidity are alleged causes, they probably act by altering the secretion, or circulation, or both, thereby lessening the normal resistance to infection ; it is not improbable that many of the previously given causes act in similar manner. Pure mycoses of the mucous surfaces may incite a catarrhal inflammation, often violent in character ; as an example of a mycotic infection, apparently restricted to the mucous membrane, thrush is most frequently cited. Bright's disease, rheumatism, gout, and allied diseases may be causes or predisposing factors. The young and aged seem more susceptible to diseases of the mucous membranes than those of middle life.

While it is not assumed that these embrace all the causes, the great majority may be embraced under some of the above. All inflammations of the mucous membranes are accompanied by a catarrhal element, just as all cutaneous inflammations are associated with some tendency to desquamation.

Morbid Anatomy.—In the first stage of the inflammation the surface is dry, or lightly covered by a thick, sticky, adherent mucus ; during life hyperemia is shown by the intense redness, which, in violent cases, may assume a dusky red ; a little later will be added evident submucous edema, from the pouring out of serum in the submucosa. The histologic

changes of this stage are engorgement of the submucous vessels and infiltration of the submucosa with serum and leukocytes; the epithelium is cloudy, swollen, and desquamating. The morbid physiology is shown in excessive dryness, giving rise, in the vocal apparatus, to the husky, rough voice or cough; in the nose, to the "stopped-up" feeling, which is intensified by the erectile tissue becoming far more distended by blood than the ordinary submucosa; in the stomach, the absence of secretion causes anorexia and nausea; in the intestines, constipation, etc.

Immediately following the first or dry stage, which may be brief or prolonged, rarely the latter, an abundant secretion of mucus occurs. The epithelial cells desquamate with the greatest rapidity, and from a dry, sticky surface, the condition changes to surface flooded with mucus. The rapidly desquamating cells undergo fatty degeneration with such promptness that the special secretion of the part is not elaborated—*e. g.*, in the stomach, no increase in pepsin; in the salivary glands, no increase in the digestive ferment, but only the abundant elaboration of mucus. The mucous membrane may fail to produce, even in small quantities, the agent which, normally, it is the function of the mucosæ to elaborate; the apepsia of gastritis may be taken as an example. The mucus is composed of the debris from the degenerating cells, including the epithelial nucleus, leukocytes, and possibly some of the serum, which is infiltrating the submucosa, may leak through the basement membrane; in very severe cases a few red blood-corpuscles escape.

The patient is usually relieved, the submucous circulation being re-established, and the perivascular exudate finding some exit by the surface and the lymphatics. If the cause be now withdrawn, the circulation gradually returns to the normal, absorption of the submucous exudate is completed, and restoration of the epithelial covering from the genetic layer

of the basement membrane gradually takes place. Ulceration rarely occurs; the basement membrane is probably never destroyed by a simple catarrhal process; when such destruction occurs, it is most likely that, during the hyperemic stage, stasis occurred in some of the vascular twigs and an ulcer followed by the process of coagulation necrosis.

(*b*) **Chronic catarrhal inflammation** of a mucous membrane results from the continuance of the last stage of the acute, or eventually persists after a succession of acute attacks. The chronic inflammations are due to a more persistent cause, usually acting from within the body—*e. g.*, the slowed circulation of chronic heart disease, the blood and vascular changes of Bright's disease, gout, rheumatism, malaria, chronic alcoholism, etc., by weakening the resistance of the mucous surface, favor repeated attacks of infection or the persistence of a single attack once developed. The continued presence of irritants also favors the process, as in the forms of pneumonokoniosis, to which we have already referred; repeated libations also weaken the mucous membrane.

Morbid Anatomy.—The continued infiltration of the submucosa with leukocytes and serum leads to permanent alterations in tissue; the leukocytes and fixed connective-tissue cells proliferate, form embryonic tissue, and this, organizing into fibrous tissue and contracting, alter the nutrition of the submucosa so that proper functional activity of the epithelial surface is more or less permanently impaired. During the earlier stages the excessive abundance of the submucous inflammatory products gives the membrane an appearance of thickening, and is often spoken of as an evidence of hypertrophy, or the inflammation is said to be *hypertrophic;* the persistent softened condition of the tube may favor dilatation in this stage; occasionally, from obstruction of ducts, mucous glands and follicles, as in the mouth, pharynx, and trachea, become

distended and prominent. The prominence of these structures has given to the process the name,—*follicular inflammation.*

As the inflammatory process advances,—grows older,—contraction of the newly-formed submucous tissue ensues, leading to lessened blood supply to the surface, faulty, perverted, or

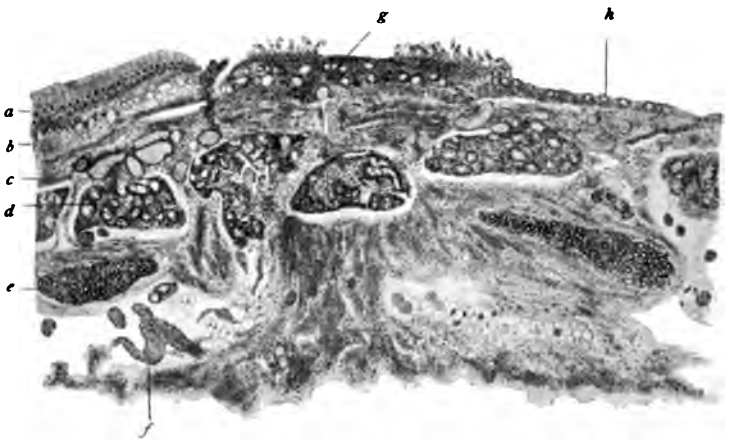

FIG. 241.—SECTION OF WALL OF BRONCHUS, CHRONIC BRONCHITIS.

Specimen hardened in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin and mounted in balsam. From slide loaned author by Professor Harris. *a*. Diagrammatic representation of the normal cylindric cells arranged normally. *b*. The line runs just under the membrana propria into a mass of newly-formed fibrous tissue, which extends downward to *e*. Just beyond the line from *c* are several blood-vessels distended by blood. *d*. Mucous gland surrounded by considerable fibroid thickening of the submucosa. *e*. Cartilage. *f*. Distended blood-vessel. *g*. Part of the chronically-inflamed mucosa with round-cell exudate in the submucosa. The normal cylindric cells which should cover the area are seen to be advancedly degenerated, desquamated, and those remaining fragmented. To the left of the lower end of the line from *g*, 1.5 cm., is depression which marks the exit point of a duct from one of the mucous glands. *h*. Denuded surface of the mucosa. Under this point, the acute inflammatory changes are less marked than at *g*. (¼-inch objective, 1-inch ocular.)

absent function of the mucous membrane, associated with thinning, an atrophy, giving the present stage the name of *atrophic inflammation;* the absence or diminution in secretion has also given the process the name of *dry catarrh.* The hypertrophic and atrophic stages of the inflammation may be seen in the same

subject at the same time, or the atrophy may be observed to follow the chronic inflammation without the development of very marked thickening, contraction exceeding in rapidity the process of infiltration. Whatever may have been the cause of the inflammation, the bacteria of decomposition find lodgment in the dry and slowly-removed secretion, and fetid or poisonous products are developed. This is illustrated in *ozena* and in chronic inflammations of the ear which have been neglected.

Sites.—There is no mucosa upon which catarrhal inflammation may not occur. The site and name for some of the accompanying catarrhal processes are as follows: Nose, rhinitis; mouth, stomatitis; tongue, glossitis; tonsils, tonsillitis; pharynx, pharyngitis; trachea, trachitis or tracheitis; bronchus or bronchi, bronchitis; in the capillary bronchi and the air-vesicles, catarrhal pneumonia—a condition in which the catarrhal inflammation differs from other localities in the tendency to accumulation, and changes in the inflammatory products and other phenomena which demand that we consider the process more in detail, as will be done when considering the forms of pneumonia; esophagus, esophagitis; stomach, gastritis, or, on account of the symptoms of indigestion, dyspepsia; colon, colitis; rectum and mucous surface of the anus, proctitis; urethra, urethritis—when due to the gonococcus it is known as gonorrhea, etc.; bladder, cystitis; ureter, ureteritis; pelvis of the kidney, pyelitis; gall-bladder, cholecystitis; gall-duct, cholangitis. Catarrhal inflammation occurs, no doubt, in the hepatic structure, but here, as in the lung and kidney, other associated phenomena demand that the condition be considered separately. Of course, the accident of location will make some differences in the character of the lesion, but the essential phenomena will be but variations of the stages and processes above indicated.

(2) **Pseudomembranous, fibrinous,** *plastic, or croupous*

inflammation of the mucous membrane. Of the many synonyms, the first two are to be preferred. The process consists

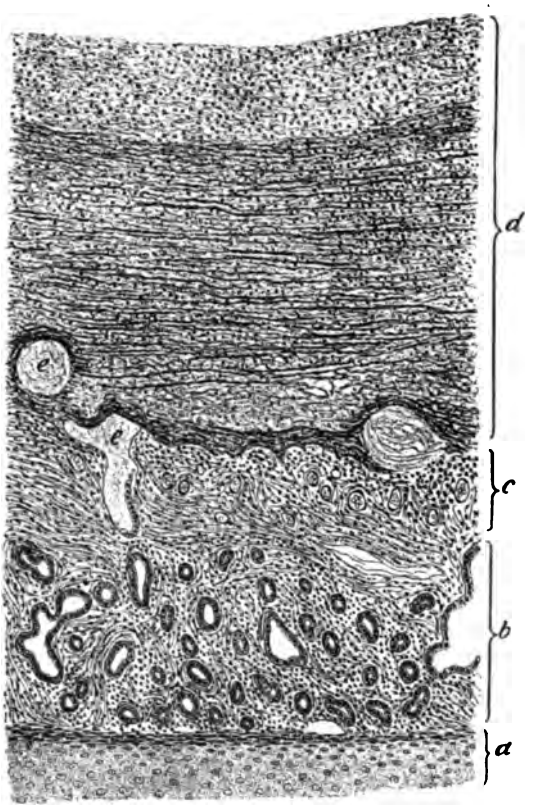

FIG. 242.—VERTICAL SECTION THROUGH THE PSEUDOMEMBRANE AND PART OF THE WALL OF THE LARYNX IN PSEUDOMEMBRANOUS LARYNGITIS.—(*Schmaus.*)

a. Cartilage. *b*. Submucosa, rich in glandular elements, also swollen and with some round-cell exudate. *c*. Line of the membrana propria. *d*. Pseudomembrane made up of fibrinous elements, in which are entangled leukocytes and desquamated fragmented epithelial cells. *e*, *e*. Gland-duct.

of an inflammation, attended by the development, on the surface of the mucous membrane, of a false or pseudomembrane composed of fibrin and entangled cell elements.

Causes.—That it can be induced without the intervention of bacteria is established, but that such is often the case is extremely doubtful. Heat, irritant gases, such as chlorin and ammonia, escharotics which do not destroy the basement membrane, and allied agents, may possibly induce an inflammation attended by the development of false membrane. Of the many alleged microbic causes, two are established: (1) the bacillus of diphtheria and (2) a streptococcus identical, morphologically, with that found in suppuration and erysipelas. Investigation into the pseudomembranous rhinitis, which often lasts for months, has demonstrated, in a large percentage of the cases, the presence of the Bacillus diphtheriæ. It would, therefore, appear that the chronic, as well as the acute, pseudomembranous inflammation, may be, in some cases at least, due to the Klebs-Löffler bacillus. Pseudomembranous inflammation of the intestine has been observed in pyemia and allied septic conditions, also in pneumonia and typhoid fever, as well as in Bright's disease, cirrhosis of the liver, and cancer (Osler). The same writer has observed membranous bronchitis in pulmonary tuberculosis, and describes a fibrinous bronchitis which arises independent of any known cause.

Morbid Anatomy.—Two forms are recognized, an acute and a chronic form; so far as known, the histology and process of development differs only in the chronic form occupying more time. Of necessity, the process begins as a catarrhal inflammation, with hyperemia and infiltration of the submucosa; liquor sanguinis passes through the basement membrane, and, reaching the surface, the necessary ferment is supplied by the bacteria or the epithelial cells (probably the latter, as the bacteria may be introduced into the circulation of an animal without immediate coagulation of the blood), and coagulation occurs.

The membrane may be fibrillar,—that is, the fibrin coagulating in fibrillæ, or branching lines,—or the result of the

coagulation may be a hyaline, homogeneous film, almost, if not quite, imperceptible; if the exudate be fibrillar, the membrane is clearly discernible during life; if hyaline, it may be

FIG. 243.—FIBRINOUS CAST FROM THE BRONCHI, CASE OF CROUPOUS PNEUMONIA.* —(*Schmaus.*)

quite invisible even in the throat. Intermediate between the fibrillar and hyaline forms of the membrane is a finely-granular

* Pneumonia is not a frequent cause of fibrinous bronchitis.

deposit resembling, to a certain extent, fragmented cells rather than a distinct fibrinous product. The membrane may be laminated, especially in chronic cases, two, three, or even four distinct layers may be shown on section; sometimes these layers do not adhere to one another and may be separated or separable; the lamination is probably due to a layer of membrane forming, followed by a pause, in which mucus forms below, and then a second layer of membrane forms and another layer of mucus, and so on, until the cavity is freed of or filled by the rapidly-forming exudate.

Occasionally, a rather extraordinary periodicity is observed in the appearance of the membrane; this is especially true of the chronic form, in which, exclusive of the pseudomembranous processes which may accompany menstruation, the membrane appears once each week, once each month, or at almost stated intervals; its appearance may be attended by fever or other symptoms; in the acute pseudomembranous inflammations this always occurs, but in the chronic types no symptoms may precede, accompany, or follow the formation of the membrane. At times a few red blood-cells may be found in the membrane. Exfoliation or casting off of the membrane may occur as rapidly as it forms, or it may remain and be pushed off by developing mucus or demanded functional activity. When removed, the surface of the basement membrane is exposed, but that tissue is not destroyed, so that the pseudomembrane may be immediately reproduced, or if the process be in a condition to terminate, the cause withdrawn, a catarrhal inflammation of the mucous surface ensues, and recovery follows exactly as in simple acute catarrhal inflammations. The tendency to re-development of the membrane in chronic cases is manifested by repeated attacks, as in membranous endometritis and membranous proctitis; in the chronic form, occurring in the bronchi, Osler says: "We know of nothing which can prevent recurrent attacks."

Sites.—There is no anatomic reason why pseudomembrane should not occur wherever catarrhal inflammation may develop. The acute pseudomembranous process is most frequent in the larynx, throat and nose, intestine, rectum, and middle ear, in the order named; the chronic is most common in the uterus, rectum, bronchi, nose, and intestine, in the order given.

(3) **Hemorrhagic inflammation** is not common on mucous surfaces. It accompanies violent infective processes like pyemia, septicemia, and specific blood mycoses like anthrax; the intoxications, such as fulminating septic peritonitis secondary to perforated ulceration in the alimentary canal (perforating gastric and duodenal ulcers); it may follow the application of cauterants like carbolic acid, etc.

Morbid Anatomy.—There is a violent inflammation of the mucous surface, attended by interstitial hemorrhage and plugging of the entire capillary area involved; there may be hemorrhage on the surface of the membrane or into the inclosed cavity. In all cases which have come to the writer's knowledge, death from other causes must have ensued, the present process being no doubt an important factor in hastening the fatal end. Should the area involved be small, it is probable that the process could terminate in the gangrenous form. The stomach and intestine are most commonly involved when the accompanying septic process is in the peritoneum. The presence of a similar condition is recognized in diphtheria, and occasionally in smallpox, occurring in the throat, trachea, nose, or mouth. The condition differs from the simple, purpuric interstitial hemorrhage, in that the latter, if recovery takes place, is absorbed in most cases without destruction or cicatrization of the mucous surface, while in the hemorrhagic inflammation, destruction invariably occurs and a scar forms to mark the site of the past process.

(4) **Gangrenous inflammation** occurs as a result of the

hemorrhagic process, or may arise from the same causes. It probably most commonly accompanies the disease diphtheria, and hence at one time was known as *diphtheric inflammation*, in contrast to the pseudomembranous or croupous inflamma-

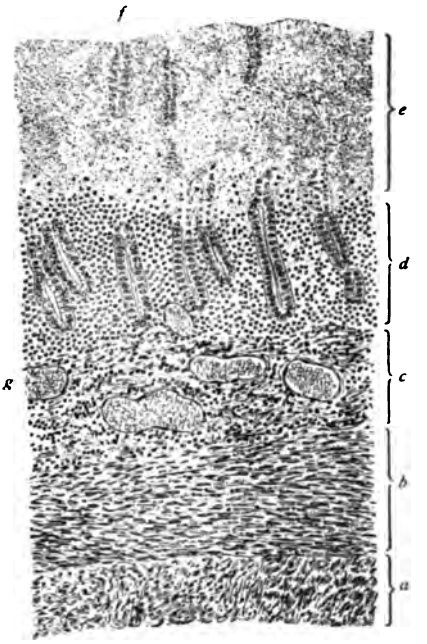

FIG. 244.—VERTICAL SECTION OF MUCOUS MEMBRANE, SHOWING DIPHTHERIC OR GANGRENOUS INFLAMMATION, FROM A CASE OF DYSENTERY.—(*Schmaus.*) × 40 diameters (?).

a, *b*. Muscular layers. *c*. Submucosa with widely-distended blood-vessels, swelling, and round-cell infiltration. *d*. Adherent portion of the mucosa in which degenerative changes are in progress, and which fades off into *e*, the necrotic layer of the mucosa. *f*. Part of a gland in the necrotic tissue, the structure of the gland elements not having been, as yet, destroyed, although separating with the necrosed layer. *g*. Distended blood-vessel.

tion, diphtheria and croup being assumed to be different diseases; we now know that the Bacillus diphtheriæ may cause both, and other inflammatory processes as well. The "*gangrenous sore throat*" and "*gangrene of the fauces*" of older

writers were types of this inflammation, and were most likely cases of diphtheria. Gangrenous inflammation also follows burns, scalds, escharotic injury, and trauma of the mucous surface. Embolic cutting off of the blood supply to an area of the mucous membrane may lead to gangrene. The writer saw a most extensive gangrenous proctitis follow the continuous use of opium and morphin by an habituate using three to six gm. of the latter each day by rectal suppository. Administration of mercury, antimony, or arsenic has been followed, in olden times, by gangrenous processes on the mucous surfaces.

It is probable that *cancrum oris*, *noma*, or *gangrenous stomatitis* is due to a bacteritic factor, although Lingard's bacillus is not generally believed to be the cause. This disease occurs in debilitated children, and usually follows one of the acute infectious diseases, and most commonly (50 per cent. of the cases) measles.

Morbid Anatomy.—Whether the initial cause be infection or not, the circulation is arrested in an area, coagulation necrosis and gangrene ensues; infection primary, secondary, or multiple is now assured, and breaking down follows. As the necrotic area extends down into the submucosa to a varying depth, the lymphatic system is widely opened and absorption of microbic poisons follows, with all the phenomena of grave septic intoxication. The plugs which occlude the vessels beome infected, break down, and hemorrhage may result; or bacteria, most commonly streptococci, gain ingress to the lymphatic system, enlargement, and even abscess formation in the nearest lymphatic gland may follow, or, reaching the blood, septicemia may ensue. The gangrene may assume phagedenic characters, and wide-spread destruction follow; this is probably due to a secondary infection, although, of course, it may have been primary, and is typified in noma, gangrenous inflammation of the labia in the female, and the

glans penis in the male ; the initial process, in the latter cases, may have been a chancre or a chancroid.

Sites.—Tonsils, pharynx, mouth, external genital organs, rectum, and colon are the most common seats, but may occur on other membranes as well. The writer has observed a very severe case of gangrenous cystitis which followed prostatic abscess with urinary infiltration.

(5) **Suppurative and pustular inflammations** occur on the mucous membranes in pyemia, septicemia, smallpox, and rarely in other infectious febrile processes. Erysipelas of the mucous membrane may be followed by suppuration. Diphtheria may, by rendering mixed infection possible, give rise to pus formation in the submucosa. Pyogenic infection of the submucosa results from abrasion or destruction of the protective epithelium, or the accumulation of infective material in a mucous gland with obstructed duct; the basement membrane of the gland being less resistant than that overlying it, rupture of the distended gland into the submucosa leads to infection and pus formation. This is probably the process which gives rise to suppurative tonsillitis and allied conditions.

Abscess in the submucosa of the urethra may follow or accompany gonorrhea. Pus, being a connective-tissue product, develops in the submucosa and secures egress, if left alone, by rupture, through gangrene or otherwise, of the basement membrane. Dissemination of the poison may occur through the lymphatics, as already described under gangrenous inflammation.

Suppurative processes are usually situated in localities liable to injury and its accompanying infection, or in membranes rich in sulci affording lodgment for materials which subsequently lead to infection; aside from the specific diseases, such as smallpox, where the pus formation occurs in pustules in the mouth and adjacent membranes, the most common seats

are in the rectum and the appendix. In the latter the infection and pus formation in the submucosa may find less resistance to egress toward the peritoneum than the mucous tract, and hence appendicitis is not uncommonly associated with infection of the peritoneum. The same obstructive conditions are present in the Fallopian tubes, and hence rupture into the peritoneum may occur more readily than escape into the uterine cavity. While the foregoing reference to appendicular and Fallopian disease is made under suppurative inflammation, it is not to be forgotten that accumulated catarrhal material contains abundant infectious agents, and its escape is as certainly followed by septic inflammation as though an abscess had poured its contents into the serous cavity. Suppurative and gangrenous processes are not uncommon in the appendix, as the writer has often seen both, and it does not seem that the Fallopian tube once infected should be less liable to the same processes.

(6) **Chronic infectious inflammations** of the mucous membranes are of the greatest importance, and deserve our closest study. For the most part they, from the beginning, involve the essential function of the mucous surface by invading the submucosa. Included under this head we have tuberculosis, leprosy, syphilis, glanders, actinomycosis, and rhinoscleroma.

Tuberculosis of the mucous membranes, independent of pulmonary tuberculosis, is not a rare condition. In the upper air-passages it is a most frequent occurrence, in tubercular patients, arising in the larynx, bronchi, and occasionally in the nose. Tuberculosis of the alimentary canal has been noted in every structure from the lips to the anus. The cause is the bacillus of tuberculosis, which has been considered in the section on "Bacteriology."

Morbid Anatomy.—Miliary tubercles develop in the submucosa, as a rule around a blood-vessel; and in marked cases

of general miliary tuberculosis, the tubercles can be seen at many points in the mucous membrane. A little later these tubercles run together and by the obliterative changes induced in the blood supply cut off the nutrition to the basement membrane and epithelium above; by this time, through confluence

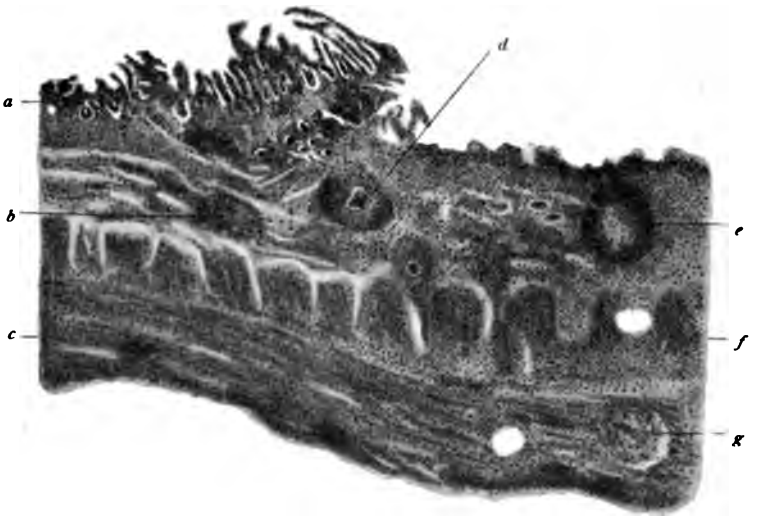

FIG. 245.—MARGIN OF TUBERCULAR ULCER OF THE INTESTINE.

Specimen hardened in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. *a*. Mucosa which, as it approaches the ulcer, is swollen, thickened with fragmented and desquamating cells. *b*, *d*, and *e*. Tubercles situated in the submucosa, *b* and *d*, and a tubercle just under and to the right of *d*, each showing a central giant-cell. The tubercle *e* shows central softening and beginning caseation. Note the extensive infiltration of the submucosa with small round-cells, which, immediately under the ulcer, at *f* have invaded the circular muscular fibers. *c*. The longitudinal muscular layer which at *g* contains a solitary tubercle. (¼-inch objective, 1-inch ocular.) Another figure illustrating tuberculosis of the mucous membrane is figure 246, page 471; see, also, illustrations in section on tuberculosis.

and softening, a cheesy area develops, and with the breaking of the basement membrane the caseous material is discharged and an ulcer results. The long axis of the ulcer is usually transverse to the long axis of the membranous tube—a condition due to the blood-vessels being distributed circumferentially

rather than longitudinally. External to the area of ulceration new fibrous tissue develops and contracts in many localities, giving rise to stenoses. When examined in its earlier stages, the condition is known as miliary tuberculosis, and later, when ulceration has ensued, or in the stage of caseation, as ulcerative or caseous tuberculosis, respectively. Rarely calcareous changes may occur and, becoming infiltrated with lime salts, the tubercle becomes quiescent, the process being arrested. The anatomy of tubercles, their method of infection, etc., has been considered with tuberculosis in general. (See "Tuberculosis," p. 221.)

Leprosy of the Mucous Membranes.—In purely anesthetic leprosy the only involvement noted by observers is in the colon, where ulcers are said to develop without leprous tubercles. Tubercular leprosy is prone to attack the mucous membranes, especially the conjunctiva, cornea, larynx, and nose. The leprous tubercles, like those of tuberculosis, occur in the submucosa and around the blood-vessels; as the process extends, the blood supply is cut off by the obliterative changes in the vessels, and a fibroid area may result; ulceration is not inevitable as in the tubercle; more commonly, however, the leprous infiltration is followed by pyogenic infective softening and ulceration. The disease is due to the Bacillus lepræ, which has been considered when dealing with bacteria (see p. 330). (For pathology of leprosy see p. 239.)

Syphilis of the Mucous Membranes.—In primary syphilis the lesion is far more frequent in the mucous membrane. The submucosa becomes infiltrated with small round-cells in which epithelioid and giant-cells may be found, the blood supply to the surface is cut off by obliterative changes in arteries, and ulceration, or rather coagulation necrosis, ensues. The roseolar rashes of the secondary stage leave no discernible lesion. The mucous patches and ulcers are the result of coagulation or liquefaction necrosis, and occur on

the tongue, pharynx, tonsils, palate, gums, and cheeks, and also on the mucosa of the anus and genital organs.

The lesions of tertiary syphilis affecting the mucous membranes are gummata occurring in the submucosa, developing like the previously-considered infective granulomata, breaking down and ulcerating; as the ulcer heals, cicatrices contracting give rise to strictures; these are most commonly seen in the larynx, rectum, and esophagus. Should cicatrization occur, without ulceration, contraction is equally sure to occur, but is less obstinate. (For pathology of syphilis see p. 219.)

Glanders.—This disease, due to the Bacillus mallei, manifests itself usually in the nose as ulcers brought about by the development of glanders nodules, made up of lymphoid and epithelioid cells in the submucosa, which, breaking down, give rise to an ulcer. In the acute form gangrenous and septic phenomena not uncommonly accompany the process; in the chronic form the ulcers may be mistaken for those due to protracted catarrhal, tuberculous, or syphilitic disease. The finding of the bacillus is essential to an accurate diagnosis. (For pathology of glanders see p. 236.)

Actinomycosis is most common in the mouth, and is due to the ray fungus or actinomyces, entrance being brought about by food containing the parasite coming in contact with an abrasion in the mucous surface. A granulation tumor made up of structures like the tubercle develops; this is usually surrounded by a zone of proliferating connective tissue which, in the jaw, has been mistaken for sarcoma. Sooner or later pyogenic infection occurs and suppuration ensues. The diagnosis can only be made by finding the fungus in the tissues or discharges. (For pathology of actinomycosis see p. 238.)

Rhinoscleroma consists in the thickening and tumefaction of the submucosa of the nose, rarely extending to the pharynx or larynx. The tumefaction begins in the nose. The tumefied areas are at first red or pink and very tender; later they

become white. The disease is due to a bacillus (see p. 321) found in the tumefied area, usually in the hyaline cells of the fibrous mesh-work. The disease is rare in this country, and clinically resembles lupus. It is essentially chronic as to time, requiring years to fully develop.

(The tumors which may occur on or in mucous membranes are numerous, and, as certain localities seem liable to given tumors, it is thought best to record the neoplasms and cysts with the special pathology of each region.)

QUESTIONS.

(1) Describe the essential histologic structures of a mucous membrane. (2) Under what conditions may hyperemia, congestion, and hemorrhage occur, and differentiate between them? (3) Define each of the following conditions, and give the lesions which accompany them: Anthracosis, (4) siderosis, (5) lithosis, (6) brown induration of the lung. (7) Give causes and morbid anatomy of an acute catarrhal inflammation. (8) How does this differ from the chronic? (9) What permanent alterations in the submucosa occur in chronic inflammations of the mucous membranes? (10) Under what conditions are these inflammations said to be atrophic? (11) Hypertrophic? (12) What inflammations of the mucosa may be due to the Bacillus diphtheriæ? (13) Of what is a pseudomembrane composed? (14) What are its most common causes? (15) Where most frequently situated? (16) What mucous surfaces are most liable to chronic pseudomembranous inflammations? (17) Give differences between hyaline, fibrillar, and laminated pseudomembranes. (18) How do pseudomembranous inflammations begin? (19) When they recover, what is the terminal stage? (20) Give causes and morbid anatomy of gangrenous inflammations of the mucous membrane. (21) How does hemorrhagic inflammation of the mucous membrane differ from purpuric interstitial hemorrhage? (22) What chronic infectious diseases occur in the mucous membranes? (23) Describe a tubercular ulcer of the larynx and give its method of development. (24) Give pathology of a gumma of the mucous membrane terminating (*a*) in a cicatrix without ulceration; (*b*) by ulceration and cicatrization. (25) What forms of leprosy occur in the larynx? (26) What are the lesions of glanders, and where do they occur? (27) How does acute glanders differ from chronic? (28) What is actinomycosis? to what is it due, and what is the character of its lesions? (29) What is rhinoscleroma?

CHAPTER V.

ORGANS OF RESPIRATION.

Anatomic divisions.—From an anatomic standpoint the organs of respiration are divided into the *nose* or *nasal cavities*, *larynx*, *trachea*, *bronchi*, and *lungs*. For physiologic consideration these are divided into the conducting part, including all but the lungs, in which the essential chemistry and vital phenomena of respiration occur. Incidentally other functions are performed by the various parts of the whole, one function being accessory to another—*e. g.*, olfaction in the nose, vocalization, etc., in the larynx, all aided by and dependent upon the various muscular and bony structures of the chest with its complex innervation.

NOSE.

Malformations.—The nose may be absent or represented by a teat or a snout-like projection in *cyclopia*, or *synophthalmia*, a malformation attended by a single orbital cavity, centrally located, and containing one or two eye-balls in varying stages of development; rarely no eye may be present. Other malformations of the nose consist in absence of one or more muscles, clefts of the alæ, deviations and faulty development of the septum, incomplete development of some of the bones entering into the formation of the cavity, constriction of the nares, more or less complete, and clefts in the floor of the nasal cavity, usually associated with faulty development of the lip, palate, or other soft parts.

Hemorrhage from the nose—epistaxis—occurs as the result of injury, either directly applied to the nasal structures,

or falls and blows severely jarring the head; extreme plethora is asserted to be a cause; hyperemia, either premonitory to inflammation or secondary to overexertion and violent cardiac action, may be a cause; violent respiratory acts like strangling, coughing, or sneezing; intracranial congestion and hyperemia; in the passive congestions of heart disease and obstructed return of blood from the head, as in tumors pressing on the veins of the neck; occasionally the hemorrhage is vicarious, as in arrested menstruation and suspended excretion —*e. g.*, sweating and suppression of urine; violent vomiting may cause it; tumors, ulcerations, etc., of the nasal mucosa; blood diseases like hemophilia, scurvy, etc. Epistaxis is also seen in the early stages of some of the acute infectious diseases, most commonly typhoid fever.

Inflammation of the nasal mucosa is spoken of as **rhinitis.** (For pathology of acute and chronic changes of inflammation and forms of inflammation of mucous membranes, see chap. IV, part III, p. 448.) Any of the already-described mucous membrane inflammations may occur in the nose. The acute catarrhal inflammation—*coryza*—is the most common. *Influenza* is commonly accompanied by a catarrhal rhinitis. *Fibrinous* and *gangrenous* inflammations of the nose may be primary or secondary to similar processes in the throat. *Tuberculosis* and *syphilis* are the most common chronic infectious inflammations; *glanders* usually here manifests itself, as does *rhinoscleroma; leprosy* and *actinomycosis* may occur. The mucosa being continuous with that of the sinuses of the superior maxilla, frontal, and ethmoid bones, and by the Eustachian tube with the middle ear, inflammation once established in the nose may extend to these structures, where, by reason of faulty drainage and inaccessibility, chronic processes ensue. The sinuses lying in proximity to the brain may afford means for intracranial infection, as seen in middle-ear disease leading to cerebral abscess, and in the tubercular meningitis asserted

to follow tuberculosis of the nasal cavities and their appendages.

Tumors.—Adult Epithelium.—*Adenomata* of the nasal mucous membrane occur more commonly as we approach the pharynx, but on the whole are not frequent; they are mostly cystic, due to inclusion of a mucous gland, ordinarily in inflammatory tissue. *Papillomata* or warts occur in the vestibule. A hairy papilloma, resting on a base of fat (lipomatous tissue), has been described. It is believed to be congenital (Arnold). Embryonic Epithelium.—*Carcinoma* of the nose is rarely primary, usually extending to the nasal cavity from the mouth or face; it is usually of the epitheliomatous type rather than glandular. Adult Connective-tissue Tumors.—*Fibromata*, *crondromata*, *osteomata*, and *myxomata* occur. True myxoma is rare, but *fibromyxoma* and pure fibroma are of not infrequent occurrence; *nasal polypi* are most commonly one of these two species. Embryonic Connective-tissue Tumors.—*Sarcomata* occur in the nasal cavity, arising from the fibrous tissue of the submucosa, the periosteum, or, rarely, the bone; they occasionally develop in the sinuses—*e. g.*, the antrum of Highmore.

Erectile tumors (*telangiectatic polypi*) are made up of numerous thin-walled blood-vessels imbedded in a fibrous, mucoid, or adenomatous matrix containing more or less myxomatous tissue. They are infrequent.

Rhinoliths are the calcareous masses occasionally found in the nose, and arise from the deposit of lime salts around a nucleus, usually a foreign body, or rarely inspissated secretion.

Anosmia, or loss of the sense of smell, may be caused by (1) central lesions, or (2) chronic catarrhal thickening, and contraction may pinch the filaments of the nerve, and thereby destroy them; a similar result may follow periosteal thickening, as seen in syphilis. When the sense is not destroyed, but perverted, the term **parosmia** is used.

LARYNX AND TRACHEA.

Normal Structure.—The epithelial layers of the mucosa vary as to depth and variety of epithelium; the epiglottis and the true cords are covered by squamous epithelium, lines of which extend between the epiglottis and cords. The greater area is covered by ciliated epithelium.

Malformations.—*Absence* of the larynx is rare. Occasionally it is small and poorly developed (*hypoplastic*), a condition said to attend testicular hypoplasia and follow castration. Abnormal largeness is at times noted. Combinations of the last-named conditions, giving rise to asymmetry, are more frequent. The ventricles may be abnormally large, or aberrant sinuses or pouches may extend into the perilaryngeal tissues, giving rise to a condition known as "*emphysema of the neck.*" From faulty union of the branchial arches fistulæ may result. Clefts and fissures of the epiglottis occur. Defects in the laryngeal cartilages are sometimes observed, but are rare.

Hemorrhage from the larynx accompanies injury, severe inflammations, tubercle, and tumors, particularly the highly vascular papillomata, and rarely from vascular distention and vicarious function.

Hyperemia occurs in the initial stage of inflammation, after violent exercise, inhalation of irritants, etc.

Congestion is noted in heart disease and lesions obstructing the return of blood from the larynx, as goiter and mediastinal tumors.

Inflammations.—Catarrhal, pseudomembranous and gangrenous inflammations occur in the order given; the latter is rare, the catarrhal common. Pseudomembranous inflammation is almost exclusively dependent upon the bacillus of diphtheria, which here rarely induces the gangrenous lesions seen on the pharynx and tonsils. Hemorrhagic inflammation is less frequent. Suppurative inflammation occurs as pustules,

as in smallpox, or as a purulent infiltration of the submucosa, most commonly secondary to an antecedent edema of the submucosa. Pus formation may be diffused in the submucosa or

FIG. 246.—TUBERCULAR ULCER OF THE MUCOUS MEMBRANE OF THE TRACHEA. VERTICAL SECTION OF THE TRACHEAL WALL.—(*Schmaus.*) × 10 diameters.

K. Cartilage. *e, e.* Epithelial layer of the mucous membrane. *t.* Tubercles in the mucous membrane. (Submucosa.) *g.* Ulcer extending from *e* to *e.*

circumscribed (abscess), in which case it may rupture into the larynx, infiltrate the perilaryngeal tissues, or dissect into the esophagus. If evacuation be established and drainage secured, repair may follow. Catarrhal, pseudomembranous, and gan-

grenous inflammations have been noted in typhoid fever, as also have suppurative and perichondroid inflammations.

The **chronic infectious inflammations** are extremely prone to invade the larynx; syphilis and tuberculosis are the most frequent, but when leprous infection or glanders occur, the larynx rarely escapes. (For morbid anatomy, etc., see chap. VII, part II; also chap. IV, part III.) Primary tuberculosis is rare, but does occur; tubercular ulcers usually are posterior and begin low and ascend, in contradistinction to syphilis which is higher and descends; cicatrization and contraction takes place in syphilis, but rarely in tuberculosis. Although rare, syphilitic and tubercular ulcers may be side * by side and differentiation of the gross lesions impossible. The finding of anatomic tubercules containing the bacillus affords the necessary evidence.

Perichondritis, or inflammation of the perichondrium, occurs as the result of acute inflammations of the mucosa; more commonly, however, it follows tuberculosis, syphilis, or inflammation, extending from surrounding structures; typhoid fever, smallpox, and, less frequently, other acute infectious processes may cause it. Pus forms in the perichondrium, escapes through the submucosa and mucosa, and an ulcer follows in which exfoliation of the cartilage takes place; the necrosed cartilage falls into the larynx and is expectorated, or it may, acting as a foreign body, fall into the bronchus, or, lodging in the air-passage at any point, give rise to acute obstruction. After exfoliation, in nontubercular cases, the ulcer tends to heal.

Calcification of the cartilages is seen in the old, rarely in the young or middle-aged.

Edema of the glottis is in most cases an inflammation. *Acute edema* follows or accompanies (1) inflammations of the

* Griffin, *The Laryngoscope*, No. 4, 1897.

mucosa as already described; (2) inflammations of adjacent tissue—*e. g.*, pharynx; (3) erysipelas and other infections not included in the previous list. It tends toward suppuration, and is therefore a true inflammatory process, probably an infection of the submucosa. *Chronic edema* may follow or precede the acute, or arise independently, and this is by far the most common. It may arise as a result of venous distention, as seen in valvular heart disease, and from compression of the veins returning from the larynx, by tumors, cysts, goiter, etc. Pulmonary emphysema, dropsical affections associated with kidney diseases or obstructive heart lesions may terminate fatally through an attack of edema of the glottis; chronic infectious processes in the vicinity are not infrequently associated with a mild degree of edema. In either form edema may threaten life by occlusion of the passage—inflammatory stenosis.

Stenosis of the larynx occurs in two forms, exclusive of the malformations—(1) functional and (2) organic. *Functional stenosis* results from paralysis of the muscles which open the larynx, or spasm of those which close it. The former most commonly results from faulty innervation due to central disease of the nerve, trunks, or brain, or pressure on the nerves by tumors, aneurysms, etc. That paralysis may follow degeneration of the muscle without antecedent nerve change seems doubtful. *Organic stenosis* follows contraction in healing ulcers, notably the syphilitic ulcerations; laryngeal tumors, edema, and inflammations; pressure from without, as in tumors and enlargements of the surrounding glands, and aneurysm; hemorrhage into the mucosa, fracture, or other injury to the laryngeal structures, as in throttling.

Tumors of the Larynx.—Adult Epithelium.—*Papillomata* are by far the most common. They may consist of fibrous as well as epithelial increase in the papilla, and be soft and dendritic, or they may be pachydermatous or hard from the

thickening and subsequent hardening. All forms of papilloma are likely to undergo transformation into cancer.

Embryonic Epithelium.—*Epithelioma* involving the larynx is usually of the squamous type, and may be dendritic like papilloma. Papillomata occur in childhood and adolescence, the cancer in middle life or later. The cylindric-cell and tubulated varieties of epithelioma also occur. In rare instances a papilloma may accompany or even follow a cancer, while the development of cancer from papilloma is not uncommon.

Adult Connective Tissue.—*Fibrous polypi*, like those described in the nose, both hard and soft, may occur in the larynx. Like the papilloma, the location is most commonly on the vocal cords. *Myxomata* are rare in the larynx, but may occur. *Chrondromata* have been observed. Embryonic connective-tissue tumors, *sarcomata* are exceedingly rare in this location.

BRONCHI.

Normal Structure.—The bronchi consist of a series of tubes lined by epithelium, columnar, and ciliated down to the terminal tubes, where the epithelium becomes cuboid; the wall of the bronchus is composed of fibrous, elastic, and a small quantity of non-striped muscular tissue, the latter being most abundant where the cartilage rings do not completely surround the tube. The mucous membrane of the larger bronchi contains numerous mucous glands.

Malformations.—Where arrest of development has occurred previous to the structural completion of the lung, the bronchi may terminate as blind pouches or may be absent. Congenital narrowing or the reverse may be found. (See "Bronchiectasis," p. 477.)

Hyperemia and congestion manifest themselves under the same conditions and with the same changes as have been elsewhere noted in the trachea, etc.

Hemorrhage. (See "Hemoptysis," p. 481.)

Inflammation.—Catarrhal inflammation, both acute and chronic, is one of the most frequent diseases of the bronchi. In the larger tubes the glands of the mucosa may stand out prominent, constituting a *follicular bronchitis*. When the inflammatory products are abundant, clear, serous fluids, the name *bronchorrhea* is given ; *bronchoblennorrhea* is applied when a puriform expectoration is present. These probably repre-

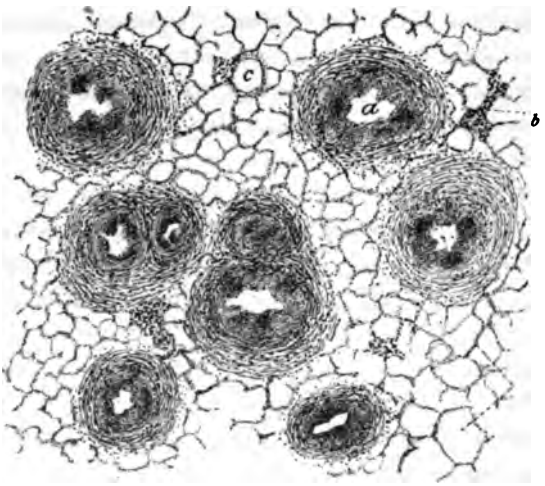

FIG. 247.—CHRONIC CASEOUS BRONCHITIS, TUBERCULOUS BRONCHITIS, CASEOUS SOFTENING OF THE BRONCHIAL WALL, WITH THICKENING OF THE PERIBRONCHIAL TISSUE, PERIBRONCHITIS CHRONICA.—(*Schmaus.*)

a. Bronchus with thickened and caseous wall surrounded by a layer of fibrinous tissue. Several other bronchi are shown, but representing slightly different degrees of the process. *b*. Transverse section of interlobular septum. *c*. Blood-vessel.

sent but different stages of the inflammatory process. *Putrid* or *fetid bronchitis* is due to decomposition of the bronchial secretion by saprophytic bacteria ; it is usually associated with bronchiectasis, the dilated cavities affording storage sufficient to permit the development of decomposition. Similar facilities are present in pulmonary gangrene, empyema with perforation of a bronchus, and in tubercular cavities, etc.

Chronic bronchial inflammation tends toward the development of fibrous tissue around the bronchi—the *peribronchitis chronica* of German writers; in other cases atrophic changes occur in the mucosa; bronchiectasis may follow; emphysema is an almost constant accompanying lesion. Of the *chronic infections*, tuberculosis is the most common; it may occur as a miliary process or as a caseous area around the bronchus which, breaking down, forms a cavity which can be only with great difficulty differentiated from bronchiectasis. *Gangrenous* and *hemorrhagic inflammations* of the bronchi are rare, and follow or accompany pulmonary gangrene, the inspiring of powerful irritants, etc.

The *fibrinous* or *pseudomembranous inflammations* of the bronchi are usually chronic, although an acute form is abundantly present in laryngeal diphtheria, fibrinous pneumonia, and less commonly in other acute infectious diseases. (For pathology of the acute, chronic, and infectious inflammations of mucous membranes see p. 448, chap. IV, part III.)

Suppurative inflammation of the peribronchial lymphatics may follow pleurisy, more especially the suppurative form (empyema), abscess, gangrene, septicemia, pyemia, and allied infectious diseases. It is not recognizable during life, and postmortem shows as a purulent infiltration of the peribronchial tissues, at times extending to the lymphatic glands; if not due to, it is usually followed by, septicemia or pyemia. (See "Pulmonary Suppuration," p. 490.)

Pigmentary infiltration of the bronchial mucosa and the effects of congestion have been studied. (See "Infiltrations of the Mucous Membranes," p. 443.)

Stenosis of the bronchi, with or without occlusion, may be due to foreign bodies, swelling of the mucosa (bronchial turgescence, as occurs in bronchial asthma), occlusion more or less complete by fibrinous exudate or mucus, pressure from peribronchial exudates, as in tuberculosis, or contraction of

newly-formed cicatricial tissue, as in syphilis, intrabronchial tumors, or pressure from neoplasms of the lung or peribronchial glands, aortic aneurysms, mediastinal tumors, and tumors of the esophagus. Atelectasis, atrophic or inflammatory changes occur in the lung tissue beyond the point of stenosis, while bronchiectasis may develop in the bronchus back of the strictured point.

Bronchiectasis, or dilatation of a bronchus, occurs in two forms, (1) *congenital* and (2) *acquired.* (1) The congenital form is unilateral, usually general, affecting many or all of the bronchi of that side (*bronchiectasis universalis*, Grawitz). The condition is a tubular or cylindric dilatation of the bronchial tubes. It is very rare and the cause but poorly understood. (2) *Acquired bronchiectasis* arises as the result of chronic bronchial inflammation, interstitial pneumonia, atelectasis, adhesions of the pleura, tuberculosis, peribronchial inflammations, usually tubercular, accumulated bronchial secretions. Two conditions are necessary in bronchiectasis : (1) Some lesion leading to softening of the bronchial wall ; (2) a distending force ; all the above offer these, and any condition inducing them may bring about dilatation. The inflammatory conditions soften the walls, and the attending cough offers the distending force ; where an area of the lung is collapsed, the bronchus delivering air to that part is subjected to inspiratory distention and commonly dilates.

The *bronchiectatic cavity* may be uniform, cylindric, or tubular, as in the bronchiectasis universale, fusiform, or spindle-shaped, saccular, globular, or irregular in outline ; the last is found in bronchiectasis due to interstitial pneumonia. As one part of the bronchial wall is nearly always weaker than some other point, the cavity is rarely symmetric. The cavity of a dilated bronchus may be eight cm., or even larger, in diameter, and from that size down to an almost inappreciable dilatation. The cavity may be differentiated from a tubercular cavity by the

following points: In bronchiectasis the wall may be smooth, lined with epithelium, and contain, at points, if not throughout, remnants of the normal bronchial wall; if the cavity be roughened by ulceration, it is at the most dependent point; the point of entrance and exit of the bronchus may be seen; no shreds of blood-vessels or other bronchi or bronchioles are to be seen in the wall or extending into the cavity; the cause may be of aid. The absence of tubercle bacilli and anatomic tubercles in the wall, of course, excludes tuberculosis.

The cavity contains accumulated secretion, and this is probably fetid, due to saprophytic infection and decomposition; ulceration may open the peribronchial lymphatics and infection of the pulmonary tissue ensue with pulmonary abscess, gangrene, etc.

Tumors of the bronchi are exceedingly rare as primary growths.

LUNGS.

Normal Structure.—The bronchi, by dichotomous division, eventually terminate in the infundibuli around which are arranged the air-vesicles. The ciliated epithelium of the bronchi become low, nonciliated, and eventually flat polygonal cells, which in turn become flat pavement-like cells in the air-vesicle. The wall of the air-vesicle is composed of fibrous and elastic tissue, in which ramify the capillaries derived from the pulmonary artery. The nutrition is dependent upon the bronchial circulation.

Malformation.—Absence of a whole lung, or a part of a lung, occasionally occurs; absence of both lungs has been observed. Additional lobes have been found present in numerous instances. Aberrant lobes, or even a miniature lung unconnected with any normal or patulous air-passage, has been observed. Hypoplastic or underdeveloped lobules or even lobes have been found, and the reverse may occur.

CIRCULATORY DISTURBANCES.

Hyperemia (active congestion or active hyperemia of some writers) occurs in violent exercise, the initial stage of acute inflammations of the lungs or pleuræ, the chill or cold stage of malarial and septic paroxysms, and allied conditions which incite powerful cardiac action; excessive heat or cold is also said to favor hyperemia; preceding death from disease of the coronary arteries, pulmonary hyperemia is alleged to occur; disease and injury of the pons or medulla are possible causes. Localized hyperemia occurs around diseased areas which interfere with the circulation, such as infarction processes, localized areas of catarrhal or croupous pneumonia, and areas invaded by any of the chronic infectious diseases to which the lung is liable.

If the lesion be purely a hyperemia, the condition to be noted in the initial stage of fibrinous pneumonia will be found.

Congestion (passive hyperemia or passive congestion of some writers) is dependent upon the slowing of the pulmonary circulation from (1) deficient force from the right heart, (2) nonaëration of the lung, (3) backing of blood from the left heart, as in valvular disease of the mitral orifice, associated with either obstruction or regurgitation, either condition permitting of increased blood-pressure within the lung. In the vast majority of cases more than one of these causes will be found acting. Two forms are constantly observed, (1) *brown induration* and (2) *hypostatic congestion*. Brown induration has already been referred to (p. 446). It arises from disease of the left heart most commonly, but may be brought about when any obstacle, beyond the pulmonary capillaries, impedes the circulation. Pulmonary edema is most commonly associated with chronic congestion.

Hypostatic congestion arises as the result of weakened heart action, deficient respiration, and gravity. It is found in febrile conditions,—*e. g.*, typhoid fever,—in the aged, after pro-

longed stay in the recumbent posture, as when a fractured limb is treated with the patient prone.

This form of congestion has also been noted in morphin poisoning and associated with, or following, disease and injuries of the brain; in the latter case the condition is further favored by deficient movement, or innervation, of the side affected, and will therefore manifest itself most likely when paralysis is present upon the affected side. All forms of coma favor the development of hypostatic congestion.

Being influenced by gravity, the dependent part of the lung shows the change; this is most commonly the posterior part. The affected area is dark in color, often almost black, much heavier than normal, pits on pressure, and when cut into blood or bloody serum streams from the cut surface; the blood may be retained in the vessels and the serum in the intervesicular structure, in which case the affected area floats in water; not uncommonly, however, the serum and even some blood permeates the vesicular wall and involves the air-vesicle, in which case areas may be selected which will sink in water; this latter condition has been called splenization and *hypostatic pneumonia*. When hemorrhage or infiltration of blood occurs in the vesicular wall, the lung may resemble diffuse pulmonary apoplexy.

The anatomy, as just given, indicates the histology. In poorly-marked cases, after hardening, very slight histologic changes may be evident, and a few leukocytes and mucous cells in excess will be found in the vesicles; the vesicular epithelium will be found cloudy and often desquamating. In more marked cases, in addition to the above, the vesicles will contain more or less blood, and infiltration of the pulmonary connective tissue by serum and blood may be demonstrable.

Pulmonary edema occurs, as already indicated, in any prolonged hyperemia or congestion, certainly the latter. It is brought about by a slowed or impeded circulation, aided by

some poorly understood alteration in the blood and, probably, in the capillary walls some degenerative change as well. It also accompanies blood dyscrasiæ, such as the various forms of anemia, Bright's disease, cancerous disease of the lung or mediastinum, and as a terminal event in the death agony when the latter is, from any cause, prolonged. Why it does not always occur in congestion, and other conditions just given, is not apparent. Aside from the general edema a local process, similar in kind, manifests itself around neoplasms, infarction, inflammatory and tubercular areas in the lung, and is spoken of as *collateral* or *circumscribed* or *localized edema.*

Morbid Anatomy.—The edematous lung is swollen, looks wet, pits on pressure, collapses slowly, if at all, is heavy but does not sink in water; on section serum flows from the cut surface, and if congestion be present, the serum is bloody.

Hemoptysis—*spitting of blood, bronchopulmonary hemorrhage. Causes:* (1) Trauma, severe falls, blows upon the chest, wounds of the lung, bronchi, etc. (2) Tuberculosis, (*a*) primary, miliary, or ulcerative lesions of the passages; (*b*) rupture of vessels, whether aneurysmal or not, in cavities. Tuberculosis is by far the most frequent cause. (3) Laryngeal, tracheal, or bronchial ulceration, arising from any cause, opening a bronchial artery. Bronchiectasis is rarely a cause. (4) (*a*) Pulmonary congestion, such as accompanies valvular heart disease; (*b*) hyperemia, as in the stage of engorgement of acute fibrinous pneumonia. (5) Malignant tumors of the lung or involving the bronchi, trachea, or larynx; papillomata of the larynx, rarely from other simple neoplasms. (6) Hemoptysis has been observed in leprosy. (7) Necrotic processes in the lung—*e. g.*, abscess, and notably gangrene. (8) Aneurysm (*a*) of the pulmonary artery or its branches, as occurs in tubercular cavities; (*b*) of the aorta; (*c*) of the innominate artery; (*d*) of the internal carotid; (*e*) of the subclavian. (9) Vicarious hemorrhage. (10) Hemoptysis in

arthritic diathesis. (11) Blood dyscrasiæ, as seen in purpura and scurvy. (12) Parasitic hemoptysis, or endemic hemoptysis, a disease common in China and Japan, due to an invasion of the lung with the Distoma Westermanni or pulmonale. (13) In a certain number of cases no assignable cause can be found: in a few of these the hemorrhage may recur a number of times without any discernible organic lesion preceding, accompanying, or following it. To this class properly belong vicarious hemoptysis, as well as that which may accompany pregnancy; in the latter instance cases are recorded in which successive pregnancies have been accompanied by recurring hemoptysis.

The effect of hemoptysis may be local or general. Locally, a slowly manifested hemorrhage may be aspirated into the air-vesicles and gradually inundate the bronchial system; a marked or severe hemorrhage may rapidly inundate and be immediately fatal. The hemorrhage may develop so slowly that no phenomena during life may be observed, and postmortem much of the lung may be found filled with the effused blood. If large cavities are present in the lung, a fatal hemorrhage may fill them and cause death without any blood spitting. The general phenomena are those of shock. The lung postmortem will be found more or less distended or inundated with blood if death occur during the attack, ante- and postmortem coagula will be found in cavities, when such are present, and in the bronchi. As the patient does not commonly die from the hemorrhage, the causes may be of more interest than the condition.

Hemorrhagic infiltration, or **infarction,** or *pulmonary embolism*, or *pulmonary apoplexy*, consists in the arrest of the circulation in a given area of the lung, vascular rhexis with infiltration of the intervesicular structure, and effusion of blood into the air-vesicles.

Causes.—Blocking of the pulmonary artery by a thrombus (autochthonous embolism) or an embolus. The latter usually

comes to the heart from the venous circulation, as in phlegmasia alba dolens, or arises in the heart, notably the right auricle. The processes of thrombosis and the origin of emboli have been considered (see chap. IV, p. 141). Where a thrombus forms, fibrinous plugs occlude the vascular supply to the affected part, and a cone-shaped area marks the outlines of the infarct.

Morbid Anatomy.—Postmortem, the changes found depend somewhat upon the extent of the area involved, the age of the infarct, and its character.

Where the lodged embolus is massive, occluding the pulmonary artery at its bifurcation, and where death occurred immediately upon its lodgment, the lung does not show the condition here considered as pulmonary apoplexy; it may show almost no change. In typic cases of recent embolism the infarct shows under the pleura as a dark-red, almost black, spot, varying in diameter from one cm. to five cm., rarely larger, and on section is found to be wedge-shaped, truly conic, with the apex of the cone directed toward the center of the lung; the color will vary from a gray, in extremely leukemic blood, to a black; as the process grows older, the color passes from black to reddish brown, and, with the gradual resorption of blood coloring-matter and resolution, the normal color may be, in favorable cases, resumed. While the typic pulmonary infarct is cone-shaped or wedge-shaped on section, the extensive anastomosis of the pulmonary circulation often affords such an abundant collateral blood-supply that the area may be almost globular, pear-shaped, and ovoid on section. The pleura over the area is at first normal, but soon shows a beginning exudate. There is usually considerable edema surrounding the infarct. If the process be not infected—it is the noninfected variety which we are now considering—and the area small, it is possible that absorption may occur. It is probable, however, that a certain amount of cicatricial tissue

always develops, and, in not a few instances, a fibroid area remains.

Histologically, the area consists of plugged vessels, with blood infiltrated into the septa and vesicles. In a short time after the infiltration the blood coloring-matter is yielded up by the red corpuscles, which also break down. The leukocytes increase in number, and, if the area involved be small, the products may pass off by the lymphatics, which, in many cases, become permanently pigmented by the process. If the area be larger, the tissue reaction greater, some fibrous tissue results; in more marked cases a puckered, pigmented, fibrous area forever marks the spot. If the bronchial artery, as well as the branches of the pulmonary artery, be occluded, the area may undergo a simple softening, fibroid change occur around it, and lime salts infiltrate it. The embolus causing the process may organize *in situ* and permanently occlude the vessels, or resolution may occur.

If the embolus contained bacteria, or should the area of the infarct become infected by the cocci of suppuration, an abscess results; if the saprophytic bacteria gain ingress and survive, gangrene may be engendered; if the embolus represented a part of a malignant tumor, a new focus of development is assured. Emboli containing the specific infectious agent of the chronic infections engender those processes in the lung. The emboli associated with the latter processes, abscess, gangrene, neoplastic growth, and chronic infections, are so small that little hemorrhagic infiltration may accompany them.

Pulmonary atelectasis occurs in two forms, the congenital and the acquired.

(1) **Congenital atelectasis,** or **apneumatosis,** is where an area of the lung does not expand following birth, but retains its fetal condition.

Causes.—Feebleness; extremely feeble infants may not be able to expand the whole lung; plugging of a bronchus by

aspirated solids, or even fluids, during delivery; imperforate bronchi, associated with the collapse, will usually show dilatation in the affected area, the extent of the dilatation depending upon the duration and force exerted.

(2) **Acquired atelectasis,** or **collapse,** is when a part of the lung which has once expanded loses its air and does not refill.

Causes.—Gas, fluids, or solids occupying the pleura, the first arising from puncture of the lung or chest wall, or both; the second from pleuritic effusions, dropsical or inflammatory, or hemorrhage into the pleura; the third from tumors. Bronchial obstruction is a most common cause; the obstruction may be a foreign body, a plug of mucus, pressure from without, as in enlarged peribronchial glands, tumors, or aneurysms. The influence of pressure may be shown in aortic aneurysm, pericardial distention, mediastinal tumors, spinal curvature, etc.; the pressure may be insufficient and the collapse not complete at first, but if the cause continues to act the collapse becomes complete.

Morbid Anatomy.—When the collapse affects the whole lung, as in pleurisy with effusion, the organ is squeezed up against the spine, is pink or pale gray in color, is firm and airless, tough, tearing with difficulty, and often can not be distended; firm adhesions may bind it down, or the pleura may have become so thickened, fibroid, and resisting that re-expansion can never occur. Where small areas of collapse occur, as in bronchopneumonia, in the recent state, they present as small depressed spots immediately under the pleura, bluish-purple or bluish-brown in color; occasionally lividity develops on exposure to the air; surrounding these areas the vesicles are distended (compensatory emphysema), and pink or reddish-white in contrast to the darker collapsed portions. If the collapse be recent and the occluded bronchus not too firmly stopped, a blowpipe, or even firm pressure on the surrounding areas,

may refill the points of collapse. Later, from stasis in the vesicular wall, the color becomes much darker, blood escapes into the connective tissue, the mass is soft and resembles the spleen in texture (**splenization**). Later, the blood is absorbed to a certain extent, the vesicular walls coalesce, proliferated connective-tissue cells and leukocytes form new fibrous tissue, and the mass is now in the condition known as **carnification.** With the completion of contraction and organization a firm fibroid area results, known as the **cirrhosis of collapse**; these areas contain a relative excess of pigment, are pink at first, later gray, and are spoken of as areas of **gray induration.**

Emphysema.—(A) **Interstitial emphysema,** also called **interlobular emphysema,** is a condition in the lung comparable to subcutaneous or surgical emphysema, as seen by the surgeon in the subcutaneous tissues in fracture of the nose, or the gas generated in the tissues in some forms of gangrene.

Causes.—(1) Ruptured air-vesicles, as occasionally occurs in violent coughing, as in whooping-cough, or in vesicular emphysema; (2) wounds of the lung, as in fractured ribs and penetrating wounds of the chest. In the latter interstitial emphysema may occur without pneumothorax, provided air does not gain ingress through the thoracic wall. Interstitial emphysema may be readily detected postmortem by the large blebs found immediately under the pleura, differing from overdistended air-vesicles in that the former can be pushed around from place to place beneath the pleura. When the rupture occurs near the root of the lung, not only does the air reach the surface of the lung by the interlobular connective tissue, but it may find access to the connective tissue of the neck.

(B) **Vesicular emphysema** is a condition in which the alveoli and infundibular passages are dilated.

(*a*) When the emphysema consists of overdistended vesicles in one area to occupy the space and receive the air intended

for another area, the condition is spoken of as **vicarious** or **compensatory emphysema.** As the condition may be acute —*e. g.*, around an atelectatic area, the withdrawal of the cause may terminate the emphysema; where the cause persists, the acute dilatation becomes permanent; at first there may be no wasting, but eventually the intervesicular septa atrophy and this form passes into true emphysema.

(*b*) **Substantive, substantial, idiopathic,** or **hypertrophic emphysema,** is a well-marked condition, readily recognized clinically, and possessing pathologic lesions eminently its own.

Causes.—There seems to be necessary a hereditary tendency, a congenital deficiency in the lung tissue, before this disease is likely to establish itself; exactly what this hereditary deficiency is has not been determined; the view that it is a defect in the elastic tissue is entirely consistent with the facts, but probably is not demonstrable. The disease is, in this sense, hereditary, it being one of the "soil" conditions transmitted from the parent. Given the first element, congenital weakness of the vesicular wall, the second is heightened intravesicular tension. This may be brought about in two ways, (1) *inspiratory* and (2) *expiratory.*

(1) *Inspiratory Distention.*—The vesicular distention of compensatory emphysema is, of course, inspiratory; and as true vesicular emphysema is almost always associated with catarrhal lesions, which favor atelectasis, the possibility of inspiratory distention acting as the cause must not be forgotten. The constant association of catarrhal inflammatory lesions and the plugging of bronchioles attended by collapse in the lobules supplied, leads to compensatory dilatation of adjacent vesicles and therefore their overdistention; the plug of mucus now shifts and another series of vesicles become overdistended. These processes frequently repeated so overdistend the elastic tissue of the vesicular wall that the normal retractile power is lost or modified and the air vesicles are thereby rendered

incompetent to fully empty themselves. (2) *Expiratory distention* acts by increased pressure applied to the lung by the bony walls, and resistance to free exit from the lung by narrowing of the laryngeal chink, glottis, epiglottidean lumen, etc.

The costal cartilages and sternum are pushed forward, the extreme normal obliquity of the ribs altered, the pulmonary space at the apex increased, thus permitting of distention of the lung at the apex or upper lobes and the anterior margins, these points showing the most marked change.

The causes active in increasing the expiratory effort are: (1) coughs, as in chronic bronchitis, the violent coughs of pertussis, etc. (2) Increased pulmonary tension, as induced by playing wind instruments, heavy lifting, etc.

Morbid Anatomy.—The chest is barrel-shaped; the cartilages calcific and rigid; when the sternum is raised, the lung does not show the normal tendency to collapse, indeed, it may not collapse at all; its anterior margins extend over the pericardium to a varying degree; when removed, it does not collapse; the pleura over the affected area is pale, anemic, dry, the unaffected areas congested; white patches occur on the pleura—the *pulmonary albinism* of Virchow; the emphysematous lines may follow the intercostal spaces, but the disease is most marked along the anterior margins, the apex, and less commonly around the margin at the base; large bullæ may be seen under the pleura, varying in size up to 0.5 or one cm., and at the free margin they may attain the size of two cm. or more.

The lung, when handled, feels like a pillow stuffed with down (Laennec). The smaller bronchi may be dilated; there is always more or less bronchitis and peribronchial induration.

The longitudinal bands of elastic tissue may be traceable in the bronchial wall.

Morbid Histology.—If the lung be blown up and dried, the enormous size of the distended vesicles may be apparent;

even on section in the recent state the atrophic remains of the vesicular walls may be discernible with a hand lens ; hardened and examined the elastic tissue will be found diminished, the vesicular septa atrophied, permitting coalescence of adjoining cells ; in the process of atrophy the capillaries disappear, and this, with the loss in septa, diminishes the aërating capacity of the lung.

Changes in Other Organs.—The increased work demanded of the right heart, in emphysema, leads to hypertrophy and

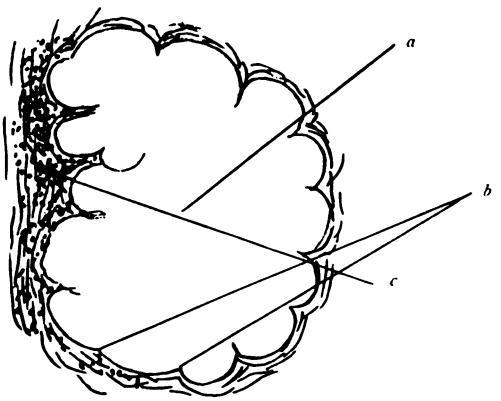

FIG. 248.—PULMONARY EMPHYSEMA.—(*Flütterer.*)

a Emphysematous enlargement of the infundibulum. *b*. Atrophied intervesicular septa, improperly called absorbed alveolar walls. *c*. Pigment in the fibrous septum.

dilatation, the former in rare cases affecting the entire heart; atheroma of the pulmonary artery with or without dilatation may occur. Other organs liable to the alterations of structure incident to venous distention usually manifest that change.

(*c*) **Atrophic** or **senile emphysema**—small-lung emphysema of Jenner—is, as its name indicates, a disease of advanced life, and is essentially an atrophic lesion of a lung in which very little, if any, distending force has been exerted.

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The chest is small, the ribs oblique, thus decreasing the diameters and diminishing the capacity of the chest; the respiratory muscles are atrophied and the lung is smaller than normal; the changes in the vesicles and septa already noted in substantive emphysema occur.

Pulmonary Suppuration.—Primary pulmonary suppuration is an exceedingly rare condition; pyogenic infection may be brought to the lung in one of four ways: (*A*) *By the air-passages;* (*B*) *from contiguous structures;* (*C*) *by the blood;* (*D*) *by the lymphatics.*

(*A*) *By the Air-passages.*—Although we are constantly inhaling large numbers of bacteria, many of them no doubt pyogenic, and pathogenic in other ways as well, the bactericidal action of the extruded epithelium, leukocytes, mucus, serum, etc., prevents ingress or pathogenic activity except the tissues be weakened by (1) *general debility*, (2) *previous local disease*, or (3) *accompanying injury*. As examples of these we have, of the first, the probability that fibrinous pneumonia in drunkards will present a mixed infection; of the second, pyogenic infection of tubercular areas, or pyogenic infection of the areas involved in lobar or lobular pneumonia, or the pyogenic infection in pneumonokoniosis. In lobar pneumonia abscess formation is rare; the so-called purulent infiltration is not really pus, as it not uncommonly contains no pneumococci, and rarely, if ever, contains the bacteria of suppuration. If abscess formation takes place in pneumonia, it usually begins as scattered foci of infection, and as such is found post-mortem; rarely, however, these foci extend and run together, the infection lessening or obliterating the circulation in the area, and more or less of a lobe may be converted into an abscess. Abscess formation in acute lobular pneumonia is still rarer.

(3) *Suppuration from injury with infection* may occur as any suppuration following an infected wound. Exploratory

puncture of the pleura has caused pulmonary abscess. But the form of infection with injury which brings infection with the injury, and both through the air-passages, is typified in the so-called aspiration pneumonia. Foreign bodies in the air-passages, suppurative processes in or around the larynx, trachea, or larger bronchi, deglutition pneumonia in which, from altered innervation, food particles gain ingress to the passages, and allied processes, may give rise to abscess formation by depositing an irritant, no matter how small, and with it the cocci of suppuration.

(*B*) *Pulmonary suppuration* arising through extension of the infection *from contiguous structures* is not common in the sense that the abscess extends by necrosis of the lung tissue, but in the lymphatics such extension may occur. Abscess of the liver or suppurating echinococcus may perforate the diaphragm and infect the lung; mediastinal abscess and other forms of peripulmonic suppuration may likewise induce pulmonary abscess. Cancer of the esophagus may lead to direct infection of the lung tissue or infection of the air-passages.

(*C*) *Pulmonary suppuration from infection through the blood* was the common sequence of pre-antiseptic surgery and obstetrics. Emboli, containing the cocci of suppuration, lodged in the lung and gave rise to centers of infection, and abscess formation ensued. These abscesses are small, usually multiple, superficially located, not uncommonly cone-shaped, with base of the cone toward the pleura, into which they not infrequently rupture, giving rise to pyopneumothorax.

(*D*) *Infection of the Pulmonary Structure through the Lymph-channels.*—An interstitial, peribronchial, or interlobular suppurative process may result from invasion of the lung tissue by way of the peribronchial lymphatics. Thus in suppurative inflammation of the pleura the lymphatics passing through the lung structure may become clogged with infective material, or material eminently adapted to infection, and cocci

accompanying this or gaining ingress to it may give rise to suppuration, which, being in the lymphatics around the bronchi, is spoken of as **peribronchial suppurative lymphangitis.** The condition can not be diagnosticated during life, and is only recognized postmortem. Pyogenic agents reaching the lung or its lymphatic system from the mediastinum or elsewhere may give rise to the process.

Morbid Anatomy of Pulmonary Abscess.—When solitary, the abscess may attain the size of a lobe ; when multiple, they are usually small. The contents, in addition to pus, will be made up of epithelial debris and remnants of lung tissue, the finding of which in the sputum is a valuable aid to diagnosis. If evacuation has occurred during life, the walls may be gangrenous and the cavity exceedingly fetid ; if the mass be small and the patient in good condition, a fibroid protecting wall may form ; ordinarily, however, the wall is made up, from within outward, of a layer of (1) necrotic breaking-down lung and inflammatory tissue ; (2) a layer of solidified lung infiltrated with leukocytes and young connective-tissue cells ; (3) edematous lung tissue. If the pleura has not been opened, the abscess wall formed by that structure will show an abundant exudate of fibrin, and some cloudy serum varying in quantity will probably occupy the cavity ; purulent pleurisy may occur without rupture of the abscess, but invariably occurs if rupture takes place, and is usually accompanied by pneumothorax, the latter depending upon whether the abscess communicates with an open bronchus. Rarely, a pulmonary abscess may encapsulate as indicated above ; in lobar pneumonia, where the evacuation is complete, cicatrization has been known to occur ; the same has taken place in hepatic abscess discharging through the lung. The majority of cases terminate fatally.

Attempts have been made to classify pulmonary abscesses from the cause as pyogenic, tubercular, actinomycotic, pneu-

monic, etc., but these are essentially mixed infections in the vast majority of cases, and the primary infection does not materially alter the essential character of the developed malady.

Gangrene of the lung consists of two elements: (1) Death of a part of the pulmonary tissue, or a material lessening of its blood supply, and (2) infection, which must be, in all probability, a mixed infection. Infection alone does not induce gangrene; obliteration of the blood supply does not insure gangrene; the two must be present. If pyogenic infection occur in a lung whose blood supply is abundant, suppuration is induced, pus being a product of vital reaction to pyogenic mycotic invasion; if, however, the tissue be dead, if vital processes be materially weakened, the tissue resistance reduced, the nutrition greatly modified by existing lesions, or, it may be, arrested, infection means gangrene.

The causes of pulmonary gangrene, then, embrace all those conditions which materially lessen or obliterate nutrition and permit infection—lobar pneumonia, aspiration pneumonia, pulmonary embolism, bronchiectasis, suppurative conditions in the lung, pressure, as from tumors and aneurysms on the bronchi and blood-vessels, etc. The cases of pulmonary gangrene which accompany or more commonly follow severe febrile processes are probably infectious in areas of hypostatic or hemorrhagic pneumonia. Brain abscess, middle-ear and mastoid disease by infectious thrombosis of the sinuses, may induce pulmonary embolism, which, being infected, will be likely to be followed by gangrene or abscess. The same is true of infectious processes in the venous system elsewhere.

Morbid Anatomy.—Two forms are recognized: *the diffuse or disseminated form*, and the *circumscribed form*. The division made, independent of any surgical view, seems aptly adapted to the modern surgical divisions of gangrene, circumscribed and spreading. The diffuse, like spreading gangrene, is rare,

and follows most commonly pneumonia, and, rarely, obstruction of the pulmonary artery.

There is not a sharp line of demarcation between the healthy and diseased tissue, a whole lobe, or the greater part of a lobe, is involved, the process well marked at the center of the disease focus but gradually fading into the surrounding zone of highly-inflamed pulmonary tissue. In the circumscribed form there is a sharp line of demarcation between the dead and the inflamed tissue, and, although the foci may be multiple, each focus is distinct from the living pulmonary tissue.

The gangrenous mass in either case is, as a rule, horribly fetid, and during life this foul penetrating odor is imparted to the breath, and persists for hours in the sputum; the latter, when left in a conic glass, separates into three layers; the uppermost is thick, frothy, yellow or green or greenish-yellow in color, the middle layer is a clear serous fluid but slightly tinted, the sediment is greenish-brown, occasionally pus-like, and contains the characteristic odor in its fullest concentration. Elastic fibers are not always present, although they usually are to be found. In the earlier stages the gangrenous tissue may retain its structure, but rapidly disintegration ensues, a cavity with ragged irregular walls forms, inclosing a green or reddish-yellow mass of softened necrotic tissue. Passing into, often across the cavity, are remains of blood-vessels and bronchi. By reason of the infectious character of the lesion, the blood-vessels do not occlude as normally by an organizing thrombus; the thrombus forming in their lumen, being infected, is easily displaced, permitting of hemorrhage which may be recurrent and in rare cases fatal. Around the gangrenous area there is a zone of deeply congested or intensely hyperemic tissue which is usually solidified, and outside of this an area of marked edema with leukocytic infiltration. Cicatrization and recovery may occur; the disease is more commonly fatal.

PNEUMONIA.

The term pneumonia is used to embrace all the inflammatory lesions of the pulmonary tissue, often including some of the lesions already considered; for example, pulmonary suppuration is sometimes spoken of as *septic pneumonia* or *suppuration pneumonia*. When used alone, without any qualifying statement, croupous pneumonia is usually meant. The forms of pneumonia commonly considered under this heading are *lobar* or *croupous pneumonia*, *catarrhal* or *bronchopneumonia*, *interstitial* or *fibroid pneumonia*, and, by some writers, the desquamative pneumonia of tuberculosis.

Lobar, croupous, or fibrinous pneumonia; *pneumonitis; lung fever*. This disease is an acute inflammatory affection of the lung due to a form of infection.

Causes.—The *exciting cause* is the diplococcus of pneumonia, first described by Sternberg as the micrococcus of rabbit septicemia. It is often found in the mouth of healthy individuals, and has been identified in the pneumonic lung, in the pleural exudate, in the pericardial fluid, in the ulcerative lesions of the endocardium, in the blood, and in the meninges in cases of pneumonia; it is also further known that while its specific lesion is in the lung, that organ may escape, and other tissues—*e. g.*, the pleura or meninges—suffer. (For description of the organism, technic of examination, etc., see chap. VIII, "Bacteriology," page 309.)

That other organisms are occasionally associated with the pneumococcus is to be expected. The cocci of suppuration gain ingress in about 30 to 40 per cent. of the fatal cases. Whether such organisms are present in the lung of nonfatal cases is extremely doubtful. Friedländer has described a bacillus which has been found alone in the lung in a small percentage of the cases examined postmortem; exactly what relation this organism bears to true croupous pneumonia is still a question not settled. That the Diplococcus pneumoniæ

of Fränkel, Sternberg, and others certainly does induce pneumonia is not doubted; that it is the exclusive cause of pneumonia seems probable, but has not been proven. In the small number of cases when the pneumococcus has not been found, it has been maintained, and with fairly sound reason, that the organism may have died or have been destroyed—a view not unsound when we consider that it is so difficult to grow, and that the tubercle bacillus, an organism whose resistance seems great, may disappear from caseous nodules in the natural course of the disease, tuberculosis.

Certain *predisposing causes* are recognized; these act in one of two ways: (1) By altering the saliva and thereby the culture medium in which the organism is growing, and these changes in the pabulum increase the virulence of the micrococcus; (2) the predisposing elements so weaken the tissues as to permit of ready infection. The latter is illustrated by the frequency with which pneumonia occurs in drunkards, in the debilitated, in Bright's disease, after contusions of the chest, etc. The latter view seems the more reasonable, and but little importance is to be attached to the first given.

All ages are liable, but pneumonia is most frequent in three periods—early childhood, between twenty and forty, and after sixty. It is more common among males than females; where both are subject to the same conditions there is little difference; conditions which disturb the equilibrium of the pulmonary circulation, as chronic heart disease; retention of excrementitious matters, as in uremia; in other words, any condition which reduces the vital powers and enables infection to occur favors the development of pneumonia. Bad hygienic conditions act in two ways—(*a*) by reducing resistance, and (*b*) by favoring the accumulation of infectious material in the surroundings. The specific cause elucidates the outbreak of occasional epidemics in crowded or unhygienic quarters. There seems to be an individual susceptibility, as explained in its frequent occurrence in

the same individual, 28 attacks having been observed in one patient (Loomis). That relapses do not occur seems to indicate a condition of acquired immunity; that such is of brief duration is also presumable from the liability to recurrent attacks. Experimentally it has been shown, in animals, that an induced immunity may be secured by the injection of filtered bouillon cultures or a glycerin extract. The immunity is temporary, lasting but a few months, but during that time is transmitted, in gestation and by nursing, to the offspring. The serum of such animals has been used with alleged success in the treatment of pneumonia.

Morbid Anatomy.—Pneumonia involves, as a rule, either a whole lobe or a whole lung, most commonly the lower right lobe; the lower left lobe is next in order; third in point of frequency is double pneumonia, while pure croupous pneumonia of the apices is rare. The right apex is more frequently involved than the left. The pneumonia is double in about 12 to 15 per cent. of the cases. The whole lobe or lung is usually in the same stage, although wandering, creeping, or migratory pneumonia, involving one lobe after another, will show different stages in different lobes; the lower lobe is most frequently involved first. In rare instances one lobe and part of another may be involved, and in different stages. Occasionally central changes precede peripheral lesions, and the center of the lung may be gray, while the periphery is less advanced —central pneumonia; rarely the reverse may be demonstrated. In double pneumonia one lung may be further advanced than the opposite organ. In infancy and old age, the apex may be more frequently the initial point; in the aged, death will, as a rule, occur earlier than in the adult. Where the disease is one-sided, the unaffected lung is deeply hyperemic and congested.

Three stages are recognized: (1) Engorgement, (2) red hepatization, and (3) gray hepatization.

Stage of Engorgement.—When the chest is opened, the organ does not retract or collapse with its wonted rapidity; there may be a slight shrinking in volume, but the general contour of the organ is likely to be retained. The lung, or the area involved, is red, often a scarlet hue. Crepitation is present throughout, but is less distinct than normal; the specific gravity is greater than normal, as shown by the fact that while the lung floats it does not float so "high" as the normal organ. On section, the color is uniform; as a rule, blood oozes from the cut surface, and while in the majority of the cases the blood is thick, flowing slowly, in some cases an abundant transudate of serum appears immediately on section, which, mixing with the blood, bathes the incised surface, and drips, or even runs, from the dependent edge.

Histology of this Stage.—On microscopic examination, the capillaries of the vesicular walls are found enormously distended, tortuous, and even saccular; the epithelium of the vesicles is swollen and, in places, desquamating; in the few vesicles with marked desquamation, some leukocytes and red blood-corpuscles may be demonstrated. The subpleural and interlobular connective tissue shows also the engorgement, and the lobules may be outlined under the pleura by the intensely engorged vessels.

This stage lasts from a few hours to two or three days; rarely the latter. It seems reasonable to suppose that in the last moments of life, or even after death has apparently occurred, solidification may develop, or, having already developed, may extend. Thus the writer has made postmortems after the most experienced clinicians had, but a few moments before death, outlined the area which seemed solid; in not a few of these cases has the solidification been found extended far beyond the outlines indicated by the physical examination made just before death. This offers some consolation for undiagnosticated areas of solidification, but it is

also explained by assuming that, after death, the lung rises as a result of retraction or partial atelectasis of the unsolidified areas above. Death rarely occurs in this stage except when great exposure, an alcoholic debauch, or other previously debilitating conditions are incident to the attack.

The stage of engorgement is often found in one part of the lung when another area is more advanced, or in one lung

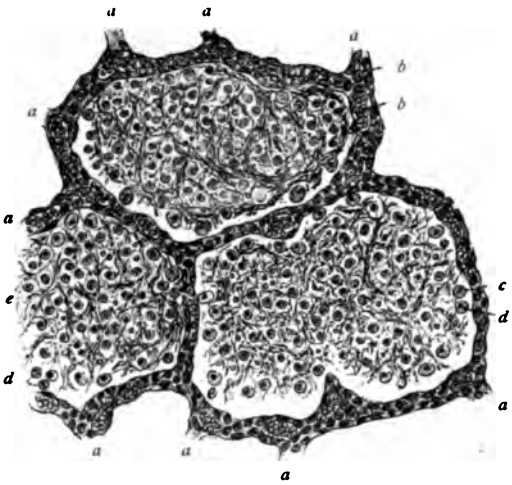

FIG. 249.—THREE ALVEOLI FILLED WITH FIBRINOUS EXUDATE. CROUPOUS PNEUMONIA, STAGE OF HEPATIZATION.—(*Schmaus.*) × 250 diameters.

a, *a*, *a*, *a*, *a*, *a*, *a*, *a*. Alveolar septa with somewhat distended capillaries, as at *b*, *b*. *c*. Meshwork of fibrin occupying the cavity of the air-vesicle. Two other air-vesicles, also filled, are shown. In this solidified exudate are entangled desquamated epithelial cells, *c*, from the alveolar wall and leukocytes, *d*, *d*.

when its fellow is solidified. It seems reasonable to assume that, in very rare cases, recovery may occur without further progress of the morbid process.

Stage of Red Hepatization.—The stage of engorgement terminates by the distended blood-vessels unloading the inflammatory exudate into the air-vesicles, and thus, by excluding the air, bringing about the stage of solidification. The lung,

or affected area, on opening the chest, shows absolutely no tendency to retract ; it is voluminous, and may be marked by the ribs ; the color is darker than the first stage, or rather more of a brown or reddish-brown ; the area involved is solid, and the absence of air is shown in the entire freedom from crepitation, in the absolute dulness and, when thrown into water, the rapidity with which the part involved sinks. On section, the organ is dry, rough, and granular ; a finger passed over the scraped surface gives the observer the impression of a rough surface, not unlike ground glass ; this and the granular appearance are due to the plugs of fibrin which occlude the vesicles and on section project ; they may be scraped out or picked out with a needle, and often an infundibulum with attached cast of the vesicles, or a bronchial plug, may be removed. The area is friable, and gives way when the finger is thrust into it ; a slice cut from the surface may break when bent ; there is nothing more characteristic than this fact. The weight of the normal lung may be 600 gm. ; the lung in croupous pneumonia may weigh three to four times as much.

Morbid Histology.—On microscopic examination the blood-vessels are less distended than in the preceding stage, although they are still fuller than normal. The inflammatory exudate poured out from the vessels now occupies the vesicular cavity. When the exudate passed from the vessel it was liquid,—liquor sanguinis,—but, in the vesicle, coagulation of the fibrin it has solidified the intravesicular contents and entangled the cellular elements present. With the transudation of the liquor sanguinis leukocytes, (diapedesis) and erythrocytes (rhexis) escape into the vesicular cavity. Thus there will be found, in the vesicle, leukocytes, red corpuscles, and a few desquamated epithelial cells entangled in a meshwork of fibrin fibrillæ. This fibrin may run as a net from point to point or show as straight lines in each vesicle ; the fibrin lines may be parallel.

From the abundance of white cells some observers have been led to suspect a beginning proliferation, especially as many of the leukocytes are polynuclear. The solid exudate extends

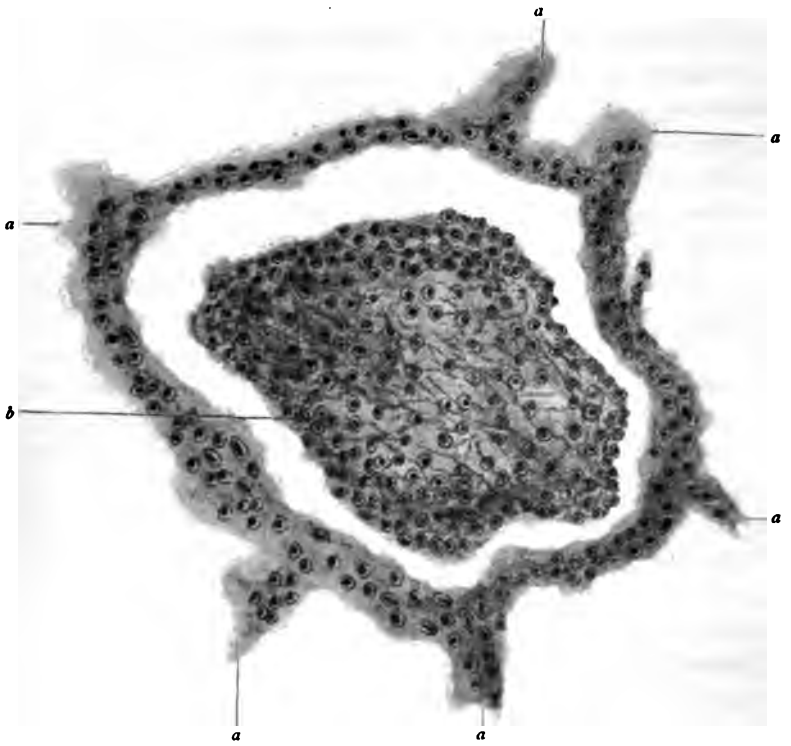

FIG. 250.—CROUPOUS PNEUMONIA. SINGLE AIR-VESICLE IN THE SECOND STAGE, WITH SLIGHTLY CONTRACTED EXUDATE. (¼-inch objective, 1-inch ocular.) Much higher magnification than in figure 249, with the object of bringing out the fibrous network.

Specimen fixed in corrosive sublimate, infiltrated with paraffin, stained with hematoxylin and eosin, and mounted in balsam. *a*, *a*, *a*, *a*, *a*, *a*. Vesicular walls. *b*. Exudate in the air-vesicle; during life the unoccupied area around the exudate either contained serum or the contraction may have occurred during fixation and hardening.

into the bronchiole, and may, in rare instances, reach bronchi of considerable size. The connective tissue of the lung also shows some change. The vesicular wall contains a number of leukocytes, but they are less abundant than in catarrhal

pneumonia. The bronchial wall is also infiltrated. Suitably prepared sections usually show abundant pneumococci, with the occasional presence of other organisms to which reference has been made.

If evidence of pleurisy did not develop in the earlier stages, it is certain to do so now. A thin plastic layer or a marked fibrinous exudate may be present. When a past pleurisy has obliterated the sac by universal adhesions, the exudate may be poured out into the adhesions, where these are not too firm. Serous exudates are rare, and, from the very nature of the lung lesion, can not be extensive.

Whether a desquamative process preceded the stage of exudation which we are now considering or not, there is now induced desquamation of the epithelial lining of the vesicles, and possibly proliferation of the leukocytes, though this is doubtful. The fibrin contracts, and free fluid collects in the vesicle or is taken up by the lymphatics. The red blood-cells undergo fragmentation, are broken up, and bronchial inflammation with some of the features of a bronchopneumonia occurs. The desquamated and fatty epithelium leads to liquefaction of the coagulum in the vesicle and the conversion of the mass into an emulsion favorable for absorption or expectoration. These changes alter the color of the organ from red to gray, and the condition is spoken of as gray hepatization. The duration of the stage of red hepatization no doubt varies; in three days after the onset of symptoms, the lung may be gray; on the other hand, the writer has examined a lung thirty-nine days after the initial chill, and thirty-seven days after the clinical diagnosis of solidification, and found the organ still red.

Gray Hepatization.—When this stage is reached, the lung no longer resembles, in its gross appearance, the previous stage, just described. As indicated, the organ is gray, yellowish-gray, or reddish-gray, depending upon the degree

to which the stage is developed; the organ is softer, and less tense, than in the red stage, tearing with the greatest ease, but less readily broken by bending. The surface is moist and smooth on section, in contrast to the dry and rough surface observed in the red stage. In gray hepatization squeezing the organ leads to a rather free flow of the partially emulsified inflammatory exudate. The peribronchial glands are enlarged, the pleurisy more advanced, and occasionally the lymphatic channels, running from the pleura toward the mediastinum, are swollen and show as light-yellow or yellowish-red streaks. The involved area is still airless, at least in the earlier stages of the gray change, as may be shown by the tests already given when considering the airless condition of the organ in red hepatization. Under the microscope no fibrin is to be demonstrated, but the vesicles are filled by cellular elements resembling those of bronchopneumonia; there are more leukocytes and desquamated epithelial cells in varying stages of granular and fatty change, and less serum than in the bronchopneumonic exudate. The coagulability of the fluids which bathe the cut surface in the gray hepatization can be shown by thrusting the organ into strong alcohol, aqueous solutions of picric or chromic acid, or boiling water, thereby coagulating the albuminous constituents of the vesicular contents. The firmness and resisting density of the red stage can not, however, be redeveloped, as the material becoming solid, at this stage, is albumin undergoing coagulation, and not fibrin.

Terminations.—It is reasonable to suppose that the gray stage is the beginning process of resolution. The softened vesicular exudate, by fatty changes, eventually becomes transformed into an emulsion which is absorbable, and sufficiently liquid to permit of being displaced from the air-vesicles and expectorated. The amount leaving the lung by absorption may be in excess of that removed by expectoration, or the reverse. When we consider the amount of the exudate

(estimated by weighing the normal lung and deducting its weight from that of the inflamed organ), varying for the entire lung between one kilo and 1800 gm., and note how little may be expectorated, we are enabled to partly appreciate the capacity of the absorbents. It is probable that this absorbed material is largely cared for by the lymphatics, as such exudates are not likely to pass through even capillary walls. The termination of lobar pneumonia in interstitial pneumonia is considered under the latter. Occasionally croupous pneumonia apparently terminates in tuberculosis. In such cases the tubercle bacillus may have been in the lung, in some quiescent nodule, or the lesion may be the result of a secondary infection in the tissues weakened by the pneumonic process. (For the formation of abscess in lobar pneumonia, see p. 490. Gangrene resulting from lobar pneumonia is also there described.)

Lesions Which May Accompany Croupous Pneumonia.—*Pleurisy* is always present in a pneumonia which reaches the lung surface. Pleurisy of the base with pneumonia of the apex, pleurisy of the opposite side, are combinations of pathologic interest. While the pleurisy is usually one of slight plastic or an abundant solid exudate and little serum, it is not invariably so ; abundant serous exudates occasionally occur, and empyema—suppurative pleurisy—is not so rare as was once believed. It is now established that the pneumococcus is the essential etiologic factor in the various forms of pleurisy, and that it may, without mixed infection, induce suppuration is probable.

Pericardial inflammation, accompanying pneumonia, partakes of the same general characteristics already described as present in pleurisy, and is due to the same cause. It occurs most commonly when the left lung is the seat of the pneumonia, and especially when that part of the lung which overlies the pericardium is the seat of the disease.

The heart muscle may show cloudy swelling, less com-

monly advanced granular change, and, rarely, a well-marked fatty degeneration may be in progress. Myocardial infective processes have not been observed. Cardiac thrombi on the left side develop rarely, except immediately preceding death, and when associated with endocardial inflammation. Just preceding death, in the agonal period, the slowed and greatly obstructed circulation of the right side may be occluded by clots extending from the right ventricle into the smaller ramifications of the pulmonary artery, and, at the postmortem, these may be pulled out as long tree- or whip-like masses.

Endocarditis, both acute simple and acute malignant, occurs. The acute simple form has been found without the observer being able to demonstrate pneumococci in the blood or cardiac lesion; they are, however, commonly present. In the malignant form of endocarditis, accompanying pneumonia, the pneumococcus is invariably present, and in a small percentage of the cases the organisms of suppuration occur in the vegetations and blood.

Monarticular joint inflammations have been frequently noted, and are extremely likely to terminate in suppuration. It is interesting to note that pneumococci have been found in these joints, in the pus from the joints, and that arthritis has been induced by the injection of the organism into a joint.

The extreme selection of serous surfaces, by this organism and its products, is further illustrated in the occasional *peritonitis* and inflammation of tendon sheaths which have been observed.

Meningitis is another illustration of the liability of serous surfaces to suffer; while it may occur with malignant endocarditis and be accompanied by embolic processes, both may be absent. The entire intracranial serous structures may be the seat of the disease, or it may be restricted to a single fossa or region, or to the base. Infection occurs through the blood or from the nasal or aural spaces, and the seat of the lesion

may indicate the source of the infection. The process may be restricted to the meninges, or the brain structure may be involved. Involvement of the spinal meninges has been observed.

Mucous membrane surfaces which may be infected by the pneumococcus, either during pneumonia or independently, and inflammatory lesions follow, are the ear (*otitis media*) and mucous surfaces of the nasal appendages—*e. g.*, *abscess of the frontal sinus*, containing the diplococcus and followed by a Diplococcus meningitis; *suppurative parotitis*, the pus containing the diplococci. Fibrinous inflammations of the stomach, colon, and other mucous surfaces may occur; hemorrhagic and gangrenous processes are less frequent except in the embolic phenomena which accompany malignant endocarditis. The epithelium of the mucosæ, liver, and kidneys is usually cloudy.

Bronchopneumonia.—This disease is also known as **lobular pneumonia,** a name objectionable in that it does not indicate the bronchial association which is always present, and also in the fact that embolic processes may be essentially lobular and still bear no relation in point of cause or pathology to the condition under consideration. The name **catarrhal pneumonia** indicates the character of the exudate, but not all of its component parts are catarrhal in point of origin, and the changes to be noted in the vesicular wall make the process more than a superficial inflammation. **Capillary bronchitis** is objectionable, as it does not indicate the accompanying vesicular change. The various other synonyms, which have been given in attempts to indicate the location or character of the lesion, the cause or termination, are either objectionable or obsolete.

Causes.—Bronchopneumonia is not, as a rule, a primary disease, but arises secondarily in some other process. In nearly if not all the cases of this disease, the bronchiole, or

the passage above, is the initial seat of the lesion, and the vesicle is secondarily affected. Where the inflammatory process follows disease of the intervesicular wall, such as tuberculosis of that structure, one can conceive the initial process to have been in the vesicle; but aside from this factor, contiguous disease, bronchopneumonia, as the name indicates, begins essentially as a bronchial inflammation.

While no specific germ has been adduced, the phenomena are those commonly attributed to infection or infectious products. The condition is so constantly associated with the various infections that it would seem that definite anatomic alterations to be described might arise from a multitude of causes, a few acting singly, or the combination of two or more factors. The fact that bronchopneumonia arises most constantly, as an important process, in the young and the aged, seems to indicate some peculiarity of tissue at those periods; this has been assumed to be, in part at least, an inability of the terminal air-passages to evacuate themselves, owing to the faulty or poorly-developed elastic tissue in the lung of the young, or muscular weakness of the respiratory apparatus in the two extremes of life; further, the epithelium of the infant, in the transitional stages of development, is most abundantly thrown off as a result of an irritation, which adult tissues would resist. That such excessive susceptibility of the mucous surfaces exists, is shown in the gastro-intestinal diseases of childhood equally as much as in the pulmonary tissues. A similar susceptibility is manifest in old age.

Bad sanitary surroundings, crowding, poorly ventilated sleeping or living rooms, are all predisposing elements. Exposure, cold, dampness, and other incidents of the winter months show a most marked influence, the disease being most abundant from November to May, inclusive, reaching its acme in the uncertain, varying, climatic conditions of the early spring months. Its relation to the infections is shown in the con-

stancy with which it develops in the presence of those conditions; of the acute infectious diseases, measles is the one with which it is most frequently associated, although diphtheria, both pharyngeal and laryngeal, especially the latter, is frequently the immediate precursor or accompanying lesion. Bronchopneumonia is commonly associated with scarlet fever and whooping-cough, less frequently with typhoid fever and small-pox.

Where the respiratory apparatus is the seat of any of the specific infectious diseases, whether acute or chronic, anthrax

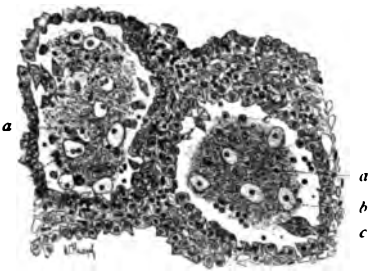

FIG. 251.—TUBERCULAR PNEUMONIA. THE DESQUAMATIVE LESION WITHIN THE AIR-VESICLES, WHICH OCCURS NEAR TO AND AROUND TUBERCLES IN THE LUNG.—(*Schmaus.*) × 250 diameters.

a, *a*. Exudate undergoing degenerative changes in the air-vesicle. *b*. Round-cells in same. *c*. Desquamating cells. The intervesicular walls are thickened.

(as in wool-sorter's disease), tuberculosis, glanders, leprosy, etc., bronchopneumonia is extremely liable to occur; and where these processes involve the lung it is inevitable. The bacillus of tuberculosis in the lung, whether in the cavities of the alveoli, as when aspirated from above, or in the vesicular or bronchiole wall, as when brought by the blood or lymphatics, always incites a bronchopneumonia which is modified by the tubercular process, but is, nevertheless, a characteristic lesion. In syphilis of the lung, bronchopneumonia may be present.

Where infectious materials are drawn into the lung, as in

the deglutition and aspiration pneumonias, to which reference has already been made, bronchopneumonia and other accompanying infective processes ensue; that bronchopneumonia is not the whole of the process is shown by the frequency with which suppuration or gangrene may follow. Bronchopneumonia also terminates fibrinous or lobar pneumonia when resolution is gradually re-establishing the normal.

In conclusion, it remains to be said that any condition which reduces the vitality of the individual, which weakens the avenues open for infection, which depresses or debilitates, favors the development of bronchopneumonia. To this group of causes belong Bright's disease, chronic heart disease, convalescence from acute processes, or the debilitating influences of more chronic ones. Bronchopneumonia always accompanies, to a varying degree, pneumonokoniosis.

Morbid Anatomy.—In recent cases, acute in time, the lung is more voluminous than normal, and does not collapse with usual promptness, and may not shrink in the least when the chest is opened; there is not that dense firmness of the tissue involved so constantly present in fibrinous or lobar pneumonia, and on superficial examination the lung appears to crepitate throughout; examined more closely, areas which do not crepitate are easily found; while firm, they are not dense, and are small nodules in contrast to the large areas of fibrinous pneumonia. On the surface of the lung near the base, as a rule, are areas sunken below the surface, blue or bluish-brown in color, usually isolated and small, although in rare instances almost, if not quite, all of a lobe may be involved in the atelectatic process. Usually such areas can be re-expanded by forcing air into the bronchus. The area joining that of collapse is not uncommonly emphysematous, as are the anterior and apical margins. At scattered points will be found projecting areas over which the pleura may be rough or even show beginning exudate. On section, the surface is usually dark or

reddish, although in adults it may be gray at points, not unlike the gray stage of fibrinous pneumonia. The surface is smooth and moist, and drips blood or bloody serum. The outline of the affected lobules can be seen, or, where a number have run together, they will usually be found in different stages, and can in that way be made out. A suitable lobule, on longitudinal section, will show the grape-like structure of the lung with alveoli, infundibula, and bronchiole filled with puriform mucus; a transverse section will show the central bronchiole, containing a tenacious plug of mucus, surrounded by distended vesicles and the adjacent collapsed lobules. Adjoining the inflamed area the areas of collapse may be well made out, or they may be indistinct; if defined, they will be dark, smooth, airless, and instead of bulging when cut, apparently retract; when immediately subpleural, there may be ecchymosis in or over them; when not well defined, the outline will show as darkish bands traversing the lobes in an irregular manner. The peribronchial lymphatic glands will be, not uncommonly, swollen and edematous, due to the effort made to carry off the degenerative product of the bronchial and vesicular inflammation.

Morbid Histology.—If a drop of the fluid which fills the air-spaces be squeezed out upon a slide, it will be found composed of germinal, granular, and fatty epithelium, with a varying number of leukocytes, rarely any red blood-cells. The fluid exudate must be solidified before making sections for histologic examination; this may be accomplished by thrusting a part of the affected tissue into boiling water, and thus coagulating the albumin in the serum and incarcerating the cellular elements; such a process alters the surrounding structures too profoundly to be commendable, and the same object may be secured by using absolute alcohol or Flemming's or Hermann's fixing solutions (see p. 42). Infiltration is imperative in order to retain the histologic structure in place.

Examination of properly-prepared sections will show the alveoli filled, not with a fibrin-bearing exudate, as in lobar pneumonia, except in a very few scattered vesicles, but a mucoid exudate containing the cellular elements indicated above, the epithelium being especially predominant. The bronchiole lumen will be found occluded by the same exudate, and the wall infiltrated by young cells, its integral elements pushed apart, typifying the swelling which was present. Longitudinal sections will show in the bronchiole, more or less irregularly in the transverse diameter, a saccular dilatation.

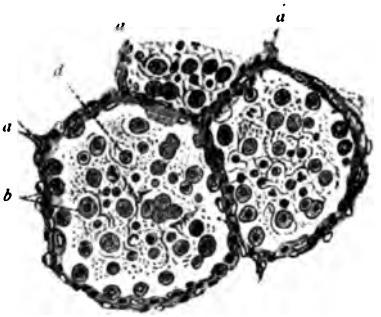

FIG. 252.—TWO ALVEOLI AND A PART OF A THIRD FROM LUNG IN CATARRHAL PNEUMONIA.

a, a, a. Walls of the alveoli. *b.* Desquamated epithelial cells from the walls of the alveolus. *c.* Alveolus filled with catarrhal exudate. *d.* Leukocyte.

The infundibulum and its surrounding vesicles are filled with a similar exudate, and the same cellular infiltration of the vesicular walls may be found. Toward the margin of the affected lobule the distention will be less marked, and the alveolar epithelium will show desquamation and marked fatty changes. The capillaries of the walls, both vesicular and bronchial, will be found distended and surrounded by leukocytes. The lymphatic channels leading from the affected areas will be engorged. In the peribronchial lymphatics more or less swelling and infiltration will be manifest.

In the bronchopneumonia which accompanies the aspira-

tion of foreign bodies into the bronchi, the bacteria present infiltrate the connective tissue, abundant leukocytic infiltration occurs, and, if the processes have sufficient time, suppuration or gangrene may ensue.

Terminations.—Acute bronchopneumonia undergoes resolution rapidly once the process begins; upon the withdrawal of the cause, the lymphatics and blood-vessels care for the unexpectorated exudate, epithelium rehabilitates the denuded walls, and organization of cellular products in the vesicular and bronchiole walls follows the removal of the liquid exudates, which cause the swelling to which reference was made while considering the histology. The feebleness of the respiration and the reduced resistance may enable deposited bacteria to secure a more or less permanent abode. That pyogenic and saprophytic bacteria may induce suppuration and gangrene has already been stated. In the distended vesicles or lobules Tubercle bacilli may lodge, and the characteristic phenomena of tuberculosis ensue, constituting a tubercular infection secondary to the bronchopneumonia. This, while possible, is no doubt rare, and where caseation with fibroid encapsulation of the caseous area is found postmortem, it is probable that the disease was tubercular from the start, but that the conservative elements limited the process; these areas may become calcareous, and exhibit the other phenomena so constantly associated with quiescent tuberculosis. It is possible for the tubercle to follow by a more wide-spread infiltration, or a wide-spread infiltration of tubercle may have induced the bronchopneumonia. At one time it was believed that caseation and fibroid change was a legitimate termination of bronchopneumonia, and recognized as a frequently occurring condition. While, as already stated, one can conceive of a simple non-tubercular area of consolidation becoming fibroid and limited, independent of the bacillus of tuberculosis, when caseation and calcareous infiltration are found the evidence is clearly that of

a "healed-in" tuberculous focus. (See "Tuberculosis of the Lungs," p. 229.)

Interstitial pneumonia, chronic interstitial pneumonia, *pulmonary cirrhosis*, or, more properly, *pulmonary sclerosis*, *fibroid induration*, *fibroid lung*, with various other synonyms, is a chronic inflammation, involving essentially the connective tissue of the organ with increase of the fibrous elements, and more or less contraction of the newly-formed tissue. The degree to which the change may progress is dependent upon many factors, and the fact that the process is secondary to other conditions has led to a multitude of names, each assuming a separate condition. No inflammation of the lung tissue, no invasion of the pulmonary structure by foreign bodies, whether coal or iron, bacteria or morbid growths, is likely to occur without a certain amount of increase in the fibrous tissue. This statement indicates the causes which are active. Fibrinous pneumonia, bronchopneumonia, tubercular pneumonia, and other infectious processes which may induce inflammation, as syphilis, leprosy, and actinomycosis, pneumonokoniosis, and inflammation of the pleura, may all be cited as etiologic factors.

The fibroid change in the lungs may involve only a small area, as where the cause is limited to that point; thus, a small, circumscribed, possibly quiescent tubercular process in an apex will be surrounded by a marked area of interstitial fibroid change. Where a protracted bronchopneumonia has involved, for any great length of time, the entire pulmonary structure, increase of fibrous tissue will be present throughout both lungs, every bronchial wall will be thickened, and every intervesicular septum more or less fibroid. Attempts have been made to classify these various stages and degrees, but one lung may be in one stage and the other show similar lesions to quite a different degree; one lung may be universally fibroid, the other show only points of fibroid change—the so-

called local fibroid pneumonia. As to source or cause, the fibrous tissue increase follows out certain lines.

In fibrinous pneumonia the area involved may not undergo resolution, but pass into this condition of fibroid change. The leukocytes and connective-tissue cells in the vesicular wall proliferate, and the fibrinous plugs which occupy the vesicles and infundibula pass through the various stages of embryonic and granulation tissues, and eventually the mass becomes converted, more or less completely, into fibrous tissue—a condition spoken of as *gray induration*. The area is gray, firm, elastic, and smooth, and looks not unlike recently developed but slightly contracted connective tissue. The process is one of the rarest terminations of croupous pneumonia. In persistent bronchopneumonia the inflammatory changes, already noted in the vesicular wall, lead to thickening, and, in the areas of collapse, this may preclude the re-establishing of function. The most marked development of fibrous tissue occurs around the bronchi,—a peribronchitis,—followed by the fibrous invasion extending to the septa between lobules, and eventually to the vesicular walls.

When fibroid lung follows an inflammation of the pleura,—*pleurogenous interstitial pneumonia*,—the condition is usually associated with plastic pleurisy, the formative inflammatory process extending into the lung by involving the interlobular septa. This differs etiologically from the fibroid condition already described, as following the more or less completely collapsed lung with thickening of the pleura and the binding down of the lung by an interstitial process; the shrinking or contraction of the lung is secondary to the development of new fibrous tissue; in the collapsed lung the fibroid change is secondary to the pleural thickening and the cessation of function.

The development of fibroid lung in pneumonokoniosis has already been referred to (see "Pneumonokoniosis," and other

infiltrations of mucous membranes, p. 433; also chronic catarrhal inflammation of mucous membranes, p. 451), and it remains only to be said that the increase in fibrous tissue, there noted, is due to the direct influence of the foreign bodies in the connective tissue of the lung, exactly as fibrous tissue develops around any extraneous body in the process of "healing-in"; to this must be added the thickening incident to the accompanying inflammation of the mucous surface, such as always occurs when persistent inflammation leads to fibrous changes in the submucosa. (See Fig. 241, p. 452.)

Morbid Anatomy.—From the above it will be seen how varied the appearance of such organs must be. In the simpler, less extensive, and generally disseminated lesion, the organ will be firmer than normal, and may show on the pleura the fibroid areas between lobes or lobules. On section, these fibrous areas will appear as gray, more or less pigmented masses, usually radiating from the central bronchus along the lines of the interlobar or interlobular septa. The uninvolved portions of the lung may be slightly emphysematous, and the elasticity of the organ so modified that it collapses slowly, if at all. In more advanced cases, or more marked fibroid change, the fibrous tissue involves a whole lobe, or a greater part of a lobe, and is conspicuous; on section, it differs but in degree from the next condition to be described, where the whole of a lung is involved.

This constitutes *true cirrhosis*, or, better, *sclerosis of the lung*. Of necessity, the process is unilateral, and the corresponding chest wall shrunken and pulled in, and the shoulder lower than that of the unaffected side. The opposite lung is voluminous, extends far past the median line, is emphysematous, and the mediastinal tissues, heart, and great vessels are pushed over to the affected part. The volume of the fibroid lung may be incredible; the author saw a case in which it was not larger than two small fists, and Osler speaks of a case in

which the affected organ was not found! The lung is firm, at times doughy and airless, and resists the knife to an unusual degree. In the pleurogenous form, and when the process follows fibrinous pneumonia, the pleura may be adherent and is always very much thickened; if the condition arose purely intrapulmonary, the pleura will possibly not be affected. The bronchi are nearly always more or less dilated, sometimes to an enormous degree (see "Bronchiectasis," p. 477). The cut surface shows the fibroid character well; the blood-vessels and bronchi are imbedded in the mass of grayish tissue. The slowness of the circulation and the loss of functional activity in the affected organ renders infection readily possible; rarely this may be pyogenic, and leave a cavity. Tuberculosis as a cause and tuberculosis as a sequence, an infection of a point of least resistance, as this truly is, occurs in no small number of cases; what relation the tuberculous process bears to the interstitial change can usually be inferred by the location and character of the lesion. The cases of tubercular origin usually show an apical cavity and some lesion of the opposite lung.

Morbid Histology.—This has been largely considered in the preceding, and varies as does the anatomy. In the less marked cases fibrous tissue in varying stages of development may be found in the vesicular walls and around the bronchi; in the advanced cases, those last considered, the bands of fibrous tissue have compressed and obliterated the pulmonary vesicles, and converted the areas involved into irregularly outlined masses of cicatricial tissue. Evidence of tuberculosis can often be demonstrated microscopically when the grosser lesions are lacking.

Termination.—Under the most favorable circumstances, in non-tubercular cases, arrest of the process is all that can be hoped for. This is dependent upon the possible removal of the cause. In a vast majority of cases tuberculosis terminates the case. The limited fibroid change, local interstitial pneu-

monia, around a point of tubercular infection, may be beneficent in that it is possible to limit the dissemination of a localized tubercular infection, and the increase of connective tissue with calcareous infiltration, as so often occurs, is no doubt the local reaction to an infection by which dissemination is prevented.

Tuberculosis of the lung arises as an (1) acute miliary process, acute phthisis, tuberculopneumonic phthisis, or galloping consumption; (2) chronic ulceration or caseous tuberculosis; (3) fibroid phthisis. Etiologically, tuberculosis arises in the lung as the result of (1) primary infection through the air-passages, or secondary infection of a bronchopneumonic area; (2) infection through the blood; (3) infection through the lymph-spaces. The various forms, anatomically and etiologically classified, have been considered with tuberculosis in general. (See "Tuberculosis of the Lungs," p. 229.)

Syphilis of the lung occurs in both the *congenital* and *acquired* forms of syphilis. In the former, a condition known as *white hepatization* is occasionally seen; proliferation of the cells which line the fetal vesicles and the connective tissue of the walls leads to the obliteration of the air-spaces, and when the inspired air, at birth, enters the lung, none gains ingress to the affected area; the only circulation to this part is that for supplying nourishment; hence, the area is pale, anemic, and known as white hepatization, the paleness contrasting with the hyperemic area which surrounds it. Another form of transmitted syphilis is the ordinary gumma. This may be found in any part of the lung, but usually near the larger bronchi at the root. These masses are usually small, but may attain the size of an orange. They are rare, and do not differ from those found in acquired syphilis.

In *acquired syphilis* gummata may be found; the situation is usually at the root of the lung, but they may be anywhere. They are gray or grayish-yellow, not uncommonly caseous, and

surrounded by a fibrous capsule, which, if recent, is translucent; if older, is firm, truly fibroid, and dense. Like all the infective granulation tumors, these begin in the alveolar walls or in the walls of the bronchi, beneath the basement membrane; after the aggregation of cellular elements, hyaline degeneration ensues, and eventually caseation completes the process and evacuation into a bronchus may follow.

In a certain number of syphilitic cases an interstitial pneumonia accompanies the gumma, and Virchow believed that a purely syphilitic process may be an interstitial inflammation beginning at the root of the lung and extending along the course of the interlobar and the interlobular septa, particularly the latter. When marked, it may be attended by bronchiectasis and all the usual phenomena of interstitial pneumonia.

Leprosy of the lung may occur as a distinctly miliary process, the leprous nodules so closely resembling those of tuberculosis that many claim that the determining factor is a tubercular infection of a leprous individual, and the almost utter impossibility of differentiating the lesions has led a few to believe that leprosy was but a form of tuberculosis; evidence to this point is not in the least conclusive, and for the present there is little doubt that the two diseases are entirely distinct.

Glanders of the lung may arise as the result of aspiration of the bacilli from lesions higher in the passage, or, as in acute glanders, the infection may occur by the blood-stream. Once localized in the lung tissue, whether interstitial or intravesicular, a more or less severe bronchopneumonia is added, and most frequently this proves fatal. When time is afforded, the typic glanders nodules develop. These lie, as a rule, immediately under the pleura, and present somewhat different aspects at different stages of their development. At first they are gray, slightly translucent, and much softer than tubercle; later they

become somewhat denser, and hyaline change occurs in the center, eventually terminating in a caseous-like encapsulated mass, especially if the process be restricted to one or two points of infection in an animal not very susceptible to the disease. In the horse, whose susceptibility is marked, and occasionally in man, the condition is likely to terminate in a suppurative pneumonia by pyogenic infection of the glanders nodules.

Actinomycosis of the lung results, in most cases, from infected material reaching the part involved through the air-passages; a bronchial inflammation accompanies the fungus down into the lobules, where a so-called miliary bronchopneumonia ensues; the number of these areas is dependent upon the number and dissemination of the fungi. A mass of granulation tissue develops around the point of infection, in which also occurs characteristic groups of fungi. Suppuration ensues, and not uncommonly cavity formation; it is claimed that the ray fungus is itself pyogenic, and can therefore induce pus formation without the intervention of the cocci of suppuration. Mediastinal actinomycosis may or may not accompany the pulmonary form, or the one may be secondary to the other. Occasionally actinomycotic fibroid changes in the lung, and "healing-in" of the area infected, may occur. In such cases the masses found postmortem are surrounded by a dense fibrous and calcareous capsule. The diagnosis of actinomycosis, both clinical and pathologic, is dependent upon finding the fungus in the sputum during life or in the masses postmortem.

Tumors of the lung are rarely primary; usually they arise by metastasis from other organs or by invasion from adjacent structures. The primary tumors are rarely of the adult epithelial type; adenoma of the bronchial glands has been described. The embryonic epithelial tumors are not correspondingly rare. It has been the author's fortune to see, within a few months, three specimens of primary cancer of the lung.

When carcinomata occur in the lung, as the result of the rich vascular supply and the relatively small amount of connective tissue, the neoplasm is most commonly encephaloid. The growth may be circumscribed and manifest itself as a few masses, or it may be but one gray, or white, soft nodule. Each nodule may grow as a single mass without very marked dissemination, but more commonly extension occurs through the lymph-channels, and the nodules become disseminated throughout the lung tissue. The local metastasis gives rise to nodules similar to the original, which, by extension, run together and convert nearly all, if not the entire, lung into a cancerous mass. Invasion of peribronchial and mediastinal lymphatics takes place, and if not fatal by this time, the process may extend to the opposite organ.

Primary tumors of the adult connective-tissue series are less rare. *Fibroma*, *chondroma*, *osteoma*, and mixed forms of these, with, rarely, a small quantity of *lipomatous* tissue, have been described. They are rarely solitary; usually a number are to be found disseminated throughout one or both lungs.

Embryonic connective-tissue tumors—*sarcomata*—occur as primary growths, but rarely. The form of sarcoma known as *endothelioma* arising, truly, in or from the pleura, is the most frequent. Like the cancers, they usually form a single large mass, but may extend to the glands and mediastinal tissues. Sarcoma as a primary tumor is restricted to one lung.

Secondary tumors of the lung arise as the result of invasion through the lymphatics or the blood; even the instances of apparently direct invasion are not truly so. It does not seem that adult epithelial-tissue tumors ever give rise to metastasis. The embryonic epithelial tumors—the cancers—very constantly do so. The epithelioma rarely, if ever; the scirrhus more commonly, and the encephaloid most frequently, arise as secondary growths in the lung. The cancers spreading by the lymphatics usually involve those structures in the lung first,

and show their dissemination along the course of the lymphatic channels. Reaching the pleura by the lymphatic system, dissemination may occur along the course of the interlobular lymphatics, in which will be seen the grayish cancerous lines traversing the connective-tissue septa, and even extending to the peribronchial glands.

Carcinoma occasionally reaches the lung by the blood, and the frequency with which this is associated with an initial focus in the digestive organs, more especially that part of the alimentary canal which communicates with the chyle duct, apparently explains this form of dissemination; in reality, the cancer element has reached the blood by being poured into the venous circulation through the lymph-channels of the abdominal cavity. When a cancerous embolus lodges in the lung, the growth immediately proceeds in the usual way; as these emboli are most commonly multiple, and fairly abundant, both lungs are likely to be involved, and many small tumors occur more frequently than a single large one. There can be found, of course, no regularity in their location, and once lodged they follow the same processes of growth and local dissemination which have already been indicated; the encephaloid cancer is the one which most frequently reaches the lung by metastasis; encephaloid cancers which have undergone colloid or mucoid change are especially liable to such dissemination. Scirrhus rarely reaches the lung.

Of the secondary tumors belonging to the adult connective-tissue series, it is said that chondromata and osteomata may reach the lung. Sarcomata—embryonic connective-tissue tumors—are the most frequent invaders, by metastasis, of the pulmonary tissues. This is due to the relation which the cellular elements of such a tumor bear to the blood-channels which course through it. The small round-cell varieties are the ones most commonly noted, although any form of sarcoma may invade the lung. As to the seat of the initial growth,

it is found that the sarcomata arising in bone, and especially in the long bones, are the most frequent growths to reach the lung. Melanotic sarcomata are also prone to such metastasis. Unlike cancers, sarcomata, if situated in the distribution of the portal vein, rarely reach the lung, but, traveling by the blood-vessels, involve the liver.

Parasites in the lung and bronchi are not of frequent occurrence. Reference has already been made to the Distoma Westermanni, Distoma pulmonale, or bronchial fluke, as a cause of hemoptysis. (See p. 481.) Ascaris lumbricoides occasionally migrates into the air-passages, and may cause obstruction, with fatal results, or, reaching the bronchi, induce gangrene, etc. It is not uncommon in infested bodies to find that the worm has entered the air-passages postmortem. *Hydatids* occur in the lung, central and subpleural. The subpleural, and hydatids of the pleura, may occur together; in either case, effusion into the pleura is usually found, and not uncommonly empyema. The cysts are multiple, and commonly near the base. They may be diaphragmatic. When in the lung, the compression resulting from their growth leads to conditions favorable to infection, and abscess or gangrene may result. Clinically and pathologically, a positive diagnosis is dependent upon finding the hooklets in the cysts or discharges. The rarer parasites found in the lung are the Cysticercus cellulosæ, Strongylus longevaginatus, Pentastoma denticulatum, etc.

QUESTIONS.

(1) What malformations may occur in the nose? (2) What is cyclopia? (3) What is epistaxis? (4) What are its causes? (5) What inflammations may occur in the nasal mucosa? (6) What is coryza? (7) What are the most common chronic infections? (8) How may diseases of the nasal addenda give rise to infections in the cranial cavity? (9) Where are these infections likely to manifest themselves? (10) Where does adenoma of the nasal cavity usually occur? (11) What type of cancer

is likely to invade the nose, and how? (12) What adult connective-tissue tumors occur in the nose? (13) From what structures do sarcomata arise in the nose? (14) What is a rhinolith? how is it formed and of what is it composed? (15) What is anosmia? (16) What is parosmia? (17) What malformations may occur in the larynx? (18) What conditions may give rise to laryngeal hemorrhage? (19) Give causes for laryngeal hyperemia and congestion. (20) To what inflammations is the larynx liable? (21) Give causes of each? (22) Give location and describe a tubercular ulcer of the larynx. (23) How does a syphilitic ulcer differ from a tubercular one? (24) What is perichondritis? to what is it due and what are its results? (25) Give causes and forms of edema of the glottis. (26) Give forms and causes of laryngeal stenosis? (27) What tumors occur in the larynx? (28) What morbid conditions may be found in the larynx? (29) Give the malformations to which the bronchi are liable. (30) What is bronchorrhea? (31) What is bronchoblennorrhea? (32) Give causes of fetid bronchitis. (33) Give causes and forms of bronchial stenosis. (34) Give form and causes of bronchiectasis. (35) How would you differentiate a bronchiectatic cavity from one due to tuberculosis? (36) Give causes of pulmonary hyperemia. (37) Give pathology of brown induration. (38) Describe a lung showing hypostatic congestion. (39) Describe a lung which is edematous. (40) Give causes of hemoptysis. (41) What is pulmonary apoplexy? (42) Describe a lung showing this change. (43) Give its histology. (44) Give its termination (*a*) if not infected; (*b*) if infected. (45) Describe a collapsed lung due to inflammation of the pleura. (46) What is emphysema and what are its forms? (47) How would you differentiate interstitial emphysema from substantive emphysema? (48) Give morbid anatomy of the latter. (49) In what forms may pulmonary suppuration occur? (50) Describe a pulmonary abscess. (51) Give causes and forms of pulmonary gangrene and describe a lung showing the changes. (52) Give predisposing and exciting causes of lobar pneumonia. (53) How may immunity to pneumonia be brought about? (54) In what order does pneumonia involve the different lobes and the two lungs? (55) What is migratory pneumonia? (56) What are the stages of croupous pneumonia, and give their order. (57) Give the morbid anatomy and morbid histology of the stage of engorgement. (58) Give same of red hepatization. (59) Give same of gray hepatization. (60) Give terminations of pneumonia. (61) What lesions may accompany pneumonia? (62) To what are they due? (63) Give synonyms for the term bronchopneumonia. (64) Give causes of bronchopneumonia. (65) What is deglutition pneumonia? (66) Give morbid anatomy of bronchopneumonia. (67) Give morbid histology, and give differences between the exudate of bronchopneumonia and

that of lobar pneumonia. (68) Give terminations of bronchopneumonia. (69) Give causes of interstitial pneumonia. (70) Give morbid histology and describe the processes by which pulmonary sclerosis develops. (71) What is pleurogenous pneumonia? (72) Describe a lung with advanced interstitial pneumonia. (73) What are the terminations of interstitial pneumonia? (74) Give the forms of pulmonary tuberculosis. (75) How may tubercular infection of the lung occur? (76) What are the forms of congenital pulmonary syphilis? (77) What are the forms of acquired pulmonary syphilis? (78) How does leprosy attack the lung? (79) What are the lesions of pulmonary actinomycosis? (80) What are the lesions of pulmonary glanders? (81) What tumors may occur in the lung? (82) How would you differentiate primary cancer of the lung from secondary cancer? (83) What kind of tumor is most likely to invade the lung by metastasis? (84) What parasite may invade the lung? (85) What morbid conditions may be found in the lung?

CHAPTER VI.

SPLEEN.

The **spleen,** in the course of the postmortem, is the first organ examined in the abdominal cavity. It varies greatly in size and weight, usually weighing between 150 gm. and 350 gm., and measuring from 10 cm. to 15 cm. in length, six cm. to ten cm. in breadth, and 2.5 cm. to 4 cm. in thickness; the relation to the weight of the body is about 1 to 360. The color varies considerably, even in health, and is influenced by the time which has elapsed since death; the same may be said of the consistency.

Malposition.—*Wandering*, or *movable, spleen* arises as a result of relaxation or stretching of its normal attachments. The extent of the displacement may be very marked, the organ at times becoming a pelvic organ. It is probable that the lengthening of the suspensory ligament may be caused by an increase in the size of the organ, and, most certainly, the organ displaced becomes larger, the increase in size being partly due to the obstruction to venous return, brought about by the tension on the splenic vein impeding the flow of blood on its way to the liver. In addition to the wandering spleen, we occasionally have, as in the liver, a partial rotation of the organ on its long axis, thus presenting an edge for percussion and other physical examination, and misleading the clinician as to the size of the organ. In the *situs inversus* the organ is on the right side.

Malformation.—The organ may be hypoplastic; there is not uncommonly a number of smaller spleens—*accessory spleens*, —which may number from one to seven or eight. Rarely, there

may be two organs of about the same size. Abnormality as to notches is common, at times the margin having from seven to ten of varying depths.

Atrophy of the spleen is said to occur. In the very old the organ is likely to be small. As a result of fibrous change, a certain amount of contraction may be present.

Hypertrophy of the spleen is seen in certain blood diseases, such as leukemia, and in acute infections the organ is not uncommonly greatly increased in size. The increase in size seen in malaria is not purely an hypertrophy.

Infiltrations.—In chronic malaria the spleen may acquire an enormous size and be intensely pigmented. The organ may weigh as much as five kilos, or even more. During the earlier infections the organ is soft, the pulp almost diffluent, and of a dark-brown chocolate color. Later, or after repeated infections, the organ becomes firmer, cutting with considerable resistance, due to a decided increase in the fibrous tissue. The color may be of a dark slate hue, due to the contained pigment. Histologically, the fibrous septa, the trabeculæ, and the pulp will all show an abundant increase, with wide-spread deposit of melanin throughout the connective tissue of the organ. This constitutes a splenic fibrosis accompanying pigmentary infiltration.

Amyloid Infiltration.—The spleen is large, and may be voluminous, weighing five kilos; it is lighter in color, of high specific gravity, with deposits of amyloid material in sago-grain-like bodies; hence, the name, *sago-spleen.* The iodin reaction renders its recognition clear. (See "Amyloid Infiltration," p. 113.) Under the microscope, the amyloid material will be seen to occupy the Malpighian bodies; in the earliest stage it probably occurs as an involvement of the arterial branch which the Malpighian body surrounds. There is a form of amyloid spleen in which the infiltration is more diffuse, not in the distinct sago grains as just described, but involving the

pulp and fibrous septa. The chemic reaction is equally well marked, but more diffuse and less punctiform than in the sago-spleen. As already described, amyloid disease arises in a number of organs almost simultaneously, but the spleen seems to suffer most in the early stage of a wide-spread morbid condition, and, for this reason, any large, rather pale organ, should be carefully tested with iodin to clearly differentiate between the enlargements, due, for example, to leukemia, and those of amyloid disease.

Splenic Engorgement.—In acute sepsis, and many of the acute infectious diseases with bacteria or their products circulating in the blood, the spleen seems to become distended with blood, its pulp soft and diffluent, the organ edematous and enlarged. This has been considered an *acute engorgement*,—an *acute hyperplasia* of the organ,—the result of the accumulation of broken-down elements, and by some a reactionary phenomenon by which the spleen, accessory to other organs, is enlarged in an effort to elaborate a power, to be manifested through the leukocytes or antitoxins, or in some other way, which may successfully combat the noxious agents circulating in the blood. As we are not fully aware of the functions of the spleen or of the organs at work in resistance against infections, the precise cause and process can not, for the present, be definitely explained.

In addition to the gross changes noted above, the tension of the capsule may be striking, and during life it may be so great that, with the softening, the organ may rupture; postmortem, such an organ is rarely removed without a tear in its capsule through which the abnormally dark grumous pulp is easily squeezed out. Such an organ will show, under the microscope, a pulp distended with blood, an enormous number of leukocytes, and the red cells advancedly fragmented. If the bacteria are circulating in the blood, the spleen may show its spaces loaded with the invaders. The

pulp-cells may be found in all stages of their life history—karyokinetic, active, cloudy, granular, and fragmenting; the displaced and softened fibrous network manifests the separation of fibers incident to edema and vascular distention.

That such organs recover there can be no doubt, as the splenic enlargement of typhoid abundantly bears out, but exactly the method of repair, restoration, and regeneration is not known. The term engorgement is not the proper one, and the term *infectious splenitis* has been offered as a substitute; the objections to the latter will be apparent when considering splenic infarctions.

Congestion of the Spleen.—In cirrhosis of the liver, with its obstructed portal circulation, and in prolapsed or wandering spleens, and in cardiac disease associated with venous distention, we not uncommonly find a large, soft, sometimes semifluctuating spleen; later the organ may be rather fibroid. The conditions are analogous to the changes found in the cyanotic kidney. There is usually a decided increase in the fibrous tissue, distended blood-vessels, edematous and rather fluid pulp, and considerable pigmentation.

Inflammation of the Spleen.—(1) **Perisplenitis.**—In general peritoneal inflammation the serous covering of the spleen is, of course, involved; by extension of inflammation from some adjacent tissue or viscus, as the stomach in chronic ulcerative processes, the diaphragm in pleurisy of the left side, perinephritic inflammations, and chronic colitis involving the splenic flexure of the colon, the capsule of the spleen may inflame, thicken, and form adhesions. Rarely do we see this as an acute process, but rather the results are seen post-mortem. The whole of the capsule may be involved (*capsular fibrosis*), or only a small area; the past inflammation is marked by a layer of inflammatory tissue two mm. to ten mm. in thickness, rarely thicker, and usually adherent to the adjacent structures, diaphragm, colon, stomach, or posterior

abdominal wall. On external examination, the white area, if small, may resemble the scar of a past infarct, but on section its purely capsular relation will be apparent. When the capsulitis has been uniformly disseminated over the whole organ, the mass, before section, may so little resemble a spleen that during an operation it has been mistaken for a tumor ; its position, relations, and attachments during life should prevent such an error, and postmortem an incision quickly shows the splenic parenchyma too clearly for error. The occasionally uniformly thickened capsule might, by contraction, lessen the splenic structure, but it is not know that such a process ever occurs to a sufficient extent to involve the function of the organ.

(2) **Splenitis.**—It is, possibly, to be admitted that, aside from bacterial causes, the spleen may suffer inflammation. Thus it is said that a splenic capsulitis, or perisplenitis, may extend into the organ and induce a parenchymatous splenitis, but the most familiar form of splenic inflammation is that associated with infarction.

Splenic Infarction.—In no organ more clearly than in the spleen is to be seen the results of lodged emboli. The vessels to the spleen are characteristically terminal, and their distribution and ending in the splenic pulp such that no embolus is likely to traverse the organ without being arrested. *Simple emboli* induce infarcts, distinctly conoid, on section wedge-shape, with, in the early stages of the process, an elevated surface, in color purplish, black, or of a combined tint, soft at first, later firm, and, again, after coagulation has terminated in liquefaction necrosis, soft, semifluid, or even cystic in consistency. Later, if not too large, organization and cicatricial-tissue formation converts the mass into a pale and eventually white cone of scar tissue extending more or less deeply into the parenchyma of the organ ; sometimes such a scar may extend down to the hilum and almost divide the organ into two parts. The number of infarcts

may be so great as to preclude counting; as a rule, there are more than one; while usually on the surface, they are not always superficial, and, while most frequently the area involved is cone-shape, the blending of a number of infarcts may offer such a misleading picture as to require careful study for positive identification.

Infected emboli quickly produce an entirely different picture. Possibly, in the early development of the infarct, the appearance is the same; soon, however, the area involved is converted into an abscess, and as such abscesses are usually multiple, the spleen becomes studded with small abscesses, or may show, by confluence, one or more of much larger size. It is well to remember that the soft, juicy, splenic pulp, with its open-mouthed blood-vessels, may contain a pus so loaded with broken-down tissue and extravasated blood as to mislead the unwary.

Coagulation necrosis, followed by fragmentation of the cells of the pulp, occurs in many infectious processes, and is almost constantly observed in the engorged organ of typhoid, diphtheria, and similar infectious diseases.

Thrombosis of the splenic vein, while rare, may occur, giving rise to edema and distention of the organ resembling the congested spleen; there is commonly more edema, and, as the process is acute, less fibrous tissue is present. The thrombus may be an extension backward from the portal vein, or, arising in the splenic vein, may extend into the portal.

Gangrene of the Spleen.—The wandering spleen may, by the twisting of its pedicle, cut off the blood supply and blood exit; the poisons produced by the disorganization of the splenic tissue favor the migration of bacteria from the adjacent alimentary canal, and, by this infection, the dissolution of the organ terminates in gangrene. The author has known two cases, undiagnosticated during life, and both found with evident infection postmortem.

Leukemia and Pseudoleukemia.—In these diseases the spleen is often much enlarged, pale or bright red, with tense capsule, and not uncommonly adhesions to the adjacent organs. In some cases the Malpighian bodies stand out as lightly-colored nodules on the incised surface, so clearly enlarged as to be most prominent features. In other cases the cut surface is uniform. Under the microscope the hyperplasia seems to involve the entire splenic parenchyma as a lymphoid cellular growth, either shown, as indicated above, by overgrowth of the Malpighian bodies and pulp, the former in excess, or of both structures without apparent differentiation.

Rupture of the Spleen.—As a result of violence, either directly applied, as by a blow or fall, or indirectly applied, as by the sudden arrest of the body, as in falling from a height, the spleen may rupture; when enlarged, the most trifling accident may be followed by laceration, and, when intensely engorged or softened, as in infectious diseases, the rupture apparently occurs without trauma—so-called *spontaneous rupture*. The hemorrhage is likely to be severe, but not invariably fatal, and in rare instances, with small stellate tears, a clot may form and the organ repair by the subsequent formation of cicatricial tissue. Rupture may occur in areas of septic infarction, splenic abscesses, and cysts.

Chronic Infections of the Spleen.— The most frequent of these is tuberculosis. It is at least questionable if *primary tuberculosis* of the organ occurs. In acute tuberculosis, with wide-spread visceral invasion, the spleen rarely escapes. At times the spleen may contain a few, or, more rarely, many tuberculous areas, five mm. to even two cm., or, in rare instances, larger caseous areas of apparently quiescent tubercle. The acute form may show as an almost uniform invasion of the organ, with typic miliary tubercles located near the arteries, in the pulp, Malpighian bodies, or even the capsule of the organ.

Syphilis of the Spleen.—In the earlier stages of syphilis the spleen may participate in the hyperplasia found in a number of the blood-making organs; later, the characteristic lesion of tertiary syphilis, the gumma, is occasionally seen. Commonly, the lesion is solitary, but in very rare cases two or more gummata may be found. The size varies greatly; the mass is spheric or oval, of a pearly- or grayish-white color, sometimes translucent, particularly at the margin. Like chronic tuberculosis, the masses are sharply defined at their margins, but, unlike the tubercular nodule, caseation is not a characteristic. In congenital syphilis a hyperplastic development of pulp or fibrous tissue at times occurs, and Ziegler records an instance in which, at birth, the enlarged spleen weighed 100 grams.

Leprosy of the spleen manifests itself as leprous nodules loaded with the bacilli in quite characteristic clusters.

Actinomycosis of the spleen occasionally occurs; with the development of the actinomycotic node, suppuration is most likely to ensue, engendering an actinomycotic abscess of the spleen.

Tumors of the Spleen.—Splenic tumors are not common. The primary tumors in an otherwise normal spleen are, of course, connective-tissue neoplasms; of the adult or typic series, angioma, fibroma, and lymphangioma are the forms usually met. Sarcoma is less rare. Secondary tumors are more frequent than the primary growths, and as sarcoma travels by the blood-stream more frequently than carcinoma, it is the usual secondary neoplasm of the spleen. Cancer, however, does occur.

Cysts of the Spleen.—More often do we find cysts than primary neoplasms. They may arise as encapsulated massive infarcts which have been unable to organize and have not been absorbed. The usual cyst is, however, of parasitic origin, and may attain considerable size; rarely the parasitic cysts of the spleen are multiple.

QUESTIONS.

(1) Give normal weight and measurements of the spleen. (2) What is wandering spleen, and to what is it due? (3) Why may the movable spleen enlarge? (4) What other malpositions of the spleen occur? (5) What malformations occur in the spleen? (6) Under what conditions may the spleen be (*a*) small? (*b*) large? (7) What infiltrations occur in the spleen? (8) Describe the spleen in malaria. (9) What is sago-spleen? (10) What is splenic engorgement? (11) What is its usual cause? (12) Give morbid anatomy and morbid histology. (13) Under what conditions may splenic congestion occur? (14) What is perisplenitis, and from what causes may it arise? (15) What is splenic capsular fibrosis? (16) What is the most frequent cause of splenitis? (17) Describe a simple infarct of the spleen. (18) What changes may it undergo? (19) What changes does the infected splenic infarct undergo? (20) In what diseases may coagulation necrosis be found in the spleen? (21) Give causes and effect of thrombosis of the splenic vein. (22) What is the most frequent cause of gangrene of the spleen? (23) What is the condition of the spleen in leukemia? (24) Under what conditions may rupture of the spleen occur? (25) What chronic infections occur in the spleen? (26) Describe tuberculosis of the spleen. (27) What lesions of the spleen may be produced by syphilis? (28) What tumors occur in the spleen? (*a*) primary? (*b*) secondary? (29) What cysts occur in the spleen?

CHAPTER VII.

LYMPH-GLANDS.*

The **lymph-glands**, or, more appropriately, the **lymph-nodes**, are, structurally, made up of a peculiar form of cell which, massed together, constitute lymphoid tissue; these, in the gland, are retained in place by a reticulum of connective tissue. The gland lies loosely in the connective tissues, and, in addition to its blood supply, receives through its capsule the afferent lymph-vessels, draining lymph from the area beyond; after passing through the gland the lymph finds its exit through the efferent vessel, eventually reaching the blood through the vein into which the lymph-vessel empties. The capsule of the gland is made up of fibrous tissue with some unstriped muscular fibers; from the capsule run septa which converge at the hilum, dividing the gland into follicles. Each follicle is made up of a reticulum, scaffolding, or sponge-like network of connective tissue, in the spaces of which are lodged the lymphoid cells; toward the periphery of the ovoid follicle the lymphoid cells are smaller than in the center, in which many of the larger form show active karyokinesis. The lymph, in passing through the gland, comes in intimate contact with the cells of the parenchyma, and in this way is probably altered in composition and cellular contents; at the same time the gland structure is exposed to whatever delete-

* The examination of the lymph-glands during a postmortem is regional; that is, we examine the glands of an area when considering other organs of the region, so that the consideration of their special pathology at this point, near the spleen, is largely due to the intimate association of their lesions with those of the spleen, rather than any special propriety of considering them at this time.

rious influences the lymph, in its return to the circulation, may bring. It will thus appear that the glands are liable to be influenced by the blood brought to them and by the lymph of the area drained.

Lymphoid Atrophy.—In the old, this process is normal. It may be a *metaplasia*, the gland being more or less replaced by adipose tissue. Such glands are usually firmer and paler than normal, and may be pigmented.

Infiltrations of Lymph-glands.—Whatever pigment the lymph may find in the tissue of the area drained, is brought to the gland, and may be there deposited. Thus, in the removal of blood extravasated into the connective tissue, the blood coloring-matter carried to the gland may be found in the cells of the gland. In anthracosis—indeed, in all forms of pneumonokoniosis—the pigment from the lung is carried to the adjacent lymph-glands, where it may be deposited to such an extent as to make the gland brown, gray, slate color, or even black. Some of the infiltrated material, as certain calcium salts, may be removed; other solid or insoluble bodies may remain as a permanent part of the gland. The infiltrated material may induce a chronic fibroid change in the gland with the production of fibrous tissue, thus rendering the gland more firm, larger, and less efficient in physiologic activity than normal. Whether normal lymph-glands are likely to be invaded by calcareous matter or not can not be definitely settled, but certainly an inflamed or infected gland is exceedingly prone to have lime deposits in its interior.

Amyloid disease affects lymph-glands as it does other tissues of the body. At times it would seem that there may be amyloid deposits in the glands of an area without manifest general deposition in other tissues. This is maintained to arise through the lymph, bringing to the gland a material which leads to the change, and which, being arrested in the gland involved, permits the other tissues to escape.

Of the *degenerative changes* in lymph-glands but little can be said. They are usually due to irritants brought to the gland, and occupy positions of secondary importance. It would seem, however, that hyaline degeneration, and possibly colloid change, may occur in lymph-nodes without any apparent or discoverable antecedent disease.

Infections of Lymph-glands.—The lymph-glands, probably more than any other tissue, possess a remarkable susceptibility to the influence of bacteria or their chemic products. There is hardly a known infection, from bubonic plague, which seems to explode its virulence on the lymph-nodes, to the most chronic infection, such as leprosy, which does not either directly or indirectly modify the structure and function of the lymphoid tissues. The change in most cases is an inflammation, a *lymphadenitis*, which may extend to the tissues around and give rise to a *perilymphadenitis*. As to time, the process may be fulminatingly acute, or extend over months or even years.

In the **lymphadenitis** arising from the ordinary infections, such as produced by the pyogenic bacteria, the appearance of the gland is greatly modified by the stage. At first it is swollen, tense, tender, and the obstruction to the passage of fluid through the gland may be evinced by a surrounding or overlying edema. On section, the surface is gray, grayish-white, or pink, or rarely there may be enough contained blood to give the cut surface a darker hue. In a gland, not previously indurated, the parenchyma is soft, and may be diffluent. Under the microscope the lymph-channels are plugged with leukocytes, and possibly fibrin; in the follicles, areas of coagulation necrosis, with fragmented cells, are usually abundantly shown. Later, the processes of degeneration extend beyond the follicles, involving the septa, and eventually the capsule and circumglandular tissues. Such an inflammatory process is spoken of as a bubo; it is common in the groin during

infectious lesions of the genitalia and superficial infections of the lower extremity; it is seen in the axilla from similar lesions of the upper extremity or mamma, and in the neck when the initial process is in the superficial tissues of the head or face. One must not forget possible unusual lymphatic distribution,—for example, cases in which involvement of the supraclavicular glands follows disease of the breast, the corresponding axillary glands escaping.

Suppuration of the lymph-glands fails to occur in many infections, particularly those in which the infecting organism does not possess the faculty of pus production. In such cases there is a degenerative change, a necrosis of the lymphoid tissue, with corresponding interference with function. Thus in diphtheria the toxins absorbed from the diphtheric area give rise to edema of the lymph-gland, coagulation necrosis, periadenoid edema, and probably lessens the phagocytic or bactericidal powers of the lymphoid tissues to such an extent as to permit of suppuration should pyogenic bacteria be carried into the gland. The somewhat dense capsule of lymph-nodes permits the occurrence of a rather lengthened intraglandular inflammation without infection of the surrounding tissue; such a battle, between the invading organism and the gland-cells, may terminate by a victory for the latter, or a drawn battle, in which case periadenoid induration and subsequent dense fibrosis, with possible calcareous change, may so surround the area of danger as to permanently include it as a "healed in" focus. It is just such a limitation that may occur in tuberculosis, as we shall see later. The gradual carrying to a gland of irritant bodies, such as may be taken up from some permanent area of infection, or as occurs in pneumonokoniosis when solid particles are being constantly thrown into the gland, induces a more or less subacute or chronic productive change, during which new fibrous tissue may be formed in and around the

gland, constituting *adenitis*, or *periadenitis chronica*, or the two forms combined.

Of the chronic infections occurring in lymph-glands, tuberculosis and syphilis are the most important, although leprosy may involve the lymphatics.

Tuberculous adenitis, the **scrofulous lymphadenitis** of the generation just past, arises from invasion of the lymph-glands by the bacillus of tuberculosis brought to the gland by the lymph- or blood-vessels. That it is usually lymphogenous can not be doubted, but this would not account for those occasional cases, truly rare, apparently no system of glands in the body seeming to escape, and in which they all develop at so nearly the same time as to preclude our saying that the initial lesion was in any one area. It may be possible that these cases are general infections directly by the blood; that is, tubercle bacilli carried throughout the organism reached the lymph-spaces, and from these were transferred to the lymph-glands. Whatever may be the cause, undoubted cases of almost universal lymphatic tuberculosis occur. The frequent form of tuberculous lymphadenitis is that of some chain of lymph-glands with a fairly clear possible source of infection. Under this head come *cervical*, *mediastinal*, *mesenteric* and *retroperitoneal*, *axillary*, and *inguinal*, *lymphadenoid tuberculosis.* The invasion, or, rather, the source of entry, can often be surmised, and, although rarely, at times demonstrated. A mucosa weakened by inflammation is the most frequent route; thus we see tuberculosis of the cervical lymph-glands following catarrhal processes of the nose or throat, or inflammatory lesions in the mouth; the frequency of mesenteric tuberculosis in bottle-fed children, where indigestive symptoms and catarrhal lesions pave the way for the entrance of the bacillus of tuberculosis (admittedly not an infrequent milk contaminant), is largely explained by admitting the increased permeability of an already diseased

mucosa. The frequency of tuberculosis of the mediastinal glands after influenza rests upon a similar basis. As already stated, the point of entry of the bacillus can sometimes be rather accurately determined. Senn reports a case in which a non-tuberculous girl wore the ear-rings of a tuberculous sister, and later developed a local tuberculous outbreak. The writer saw a case of axillary tuberculosis follow a wound made by a corset steel on the outer margin of the breast in a young girl nursing a sister advanced with tuberculosis of the lungs; the glands were removed, and no further evidence of tuberculosis has been observed.

With the deposit of the tubercle bacilli in the lymph-node the evidence of infection begins. There is quickly developed an epithelioid cellular accumulation arising by a proliferation of the endothelial cells of the lymph-paths; to these are added the polynuclear leukocytes which, with probably some multiplication of the lymphoid cells, gives us the anatomically mature tubercle. A number of these run together, caseation occurs, local diffusion, involving the whole gland, followed by a periadenitis which mats the glands of the area together, a condition which the surgeon dislikes not a little, the infection spreading to the circumadenoid tissues and, eventually, by the route of least resistance, reaches the skin. During this time it is possible that some of the bacilli may have passed the gland and assured further extension of the process by a second incursion through the lymph-stream. The course just described may be arrested at any point. The bactericidal action of the lymphoid structures, including the leukocytes, may terminate the process by a victory, the bacilli succumbing or becoming so surrounded by a protective cordon of leukocytes as to limit the lesion to the area involved, or, possibly, to a single gland, or even a part of a gland. This "healing in" of a gland, part of a gland, or a mass of glands, does not represent a cure, but merely a quiescent infection which may, when the protective

power is weakened by some secondary or intercurring malady, break out anew.

During the early stage of the process, if such a gland be examined, it will be found swollen, with but slight hyperemia, and such little macroscopic evidence of tuberculosis as to make a study of its histology necessary. Later, when by confluence and caseation the parenchyma of the lymph-gland is converted into multiple centers of caseation, or, later, when we have a more advanced change converting the gland into a caseous mass, the recognition is easy. (For morbid anatomy and general description of tuberculosis of lymph-glands see p. 227.)

Syphilitic Lymphadenitis.—The nearest anatomic lymph-node, draining an area in which there is an initial lesion of syphilis, shows, as a rule, a reaction to the invasion, which is quickly followed by surrounding glands and, eventually, in the vast majority of cases, by the lymphadenoid tissues at large. This initial or primary glandular involvement seems to be almost purely a proliferative change in the cells of the lymphoid follicle and further blocking by leukocytes. The change is usually transitory, and disappears in a few days under treatment and, often, in a few weeks without. In addition to this primary involvement of the glands we may have gummata in an active stage of development, or gummatous changes represented by atrophied, cicatrized, or caseous areas of a practically cured tertiary glandular change.

Under the name of **lymphadenia, lymphadenoma, lymphosarcoma, progressive lymphadenoid hyperplasia, malignant lymphoma, simple adenia, Hodgkin's disease, pseudoleukemia,** and other more or less synonymous terms, there exists a peculiar form of lymphoid change in which one or more of the lymphadenoid tissues of the body are involved, including not only the lymph-glands, the spleen, and tonsils, but even the lymphoid tissues of the various mucosæ.

The tendency at present is to regard the group as truly sarcomatous, and but little effort is being made at the present time to separate such glandular enlargements from the admittedly malignant growth—the sarcomata of lymphatic glands.

The enlarged glands are white, or grayish-white, and are either firm or soft, depending upon the rapidity of their growth; in rare cases there may be evidence of necrosis in their interior. As a rule, they remain distinct until reciprocal pressure has coalesced them, and not until they have attained considerable size do they show evidence of periadenoid extension; to this there are notable exceptions, and occasionally, in a group of glands, many differences in consistency, color, and evidences of infiltration may be present. When examined under the microscope, much difficulty will be found in attempting to classify these growths. In some there may be naught but the true structure of a lymph-node on a large scale,—a true lymphoid hyperplasia,—while in others the resemblance to a normal gland can be observed only with the greatest care; between these two extremes all stages in lymphoid-tissue proliferation may be demonstrable; the gland capsule may be intact, or it may be infiltrated and the same cellular texture may be demonstrable from one gland to another.

Tumors of Lymph-glands.—If we except the foregoing enlargements from the tumors of lymph-glands, the only primary tumor of the lymph-node is the *sarcoma;* the alveolar, round-cell, melanotic, and mixed-cell forms occur in the order given. Sarcoma may be secondary as well as primary, but is less commonly so. The frequent secondary tumor of lymph-glands is cancer. In all its forms, *carcinoma* involves the lymph-spaces; the extent of this involvement of the primitive lymph-paths and the portability of the invading cells, together with the resistance of the individual, determine the rapidity with which the tumor-cells reach the lymph-gland. Thus the rapidly growing, almost spheric, cells of

the encephaloid spread more rapidly than the squamous, or flat, irregular cell of the epithelioma. (See "Tumors," chap. VI.) When the lymph-node is reached, the histology of the primary tumor is usually as fully reproduced as the gland and its surrounding structure will admit.

QUESTIONS.

(1) Give normal structure of lymph-node. (2) What lymphatic change occurs in the old? (3) What is the most frequent infiltration of lymph-glands? (4) Under what conditions may pigmentation of lymph-glands occur? (5) What other infiltrations occur, and under what conditions? (6) What lesions occur in lymph-glands as a result of infection? (7) Describe a lymph-gland showing lymphadenitis. (8) Give its histology. (9) What is a bubo? (10) What changes occur in lymph-glands as the result of toxins without bacteria? (11) Give morbid anatomy and morbid histology of a lymph-gland showing tuberculosis. (12) What is the usual source of infection of lymph-glands by tuberculosis? (13) What results may be seen in a lymph-gland indicating a past tuberculosis? (14) What change occurs in the lymph-gland in syphilis? (15) Give synonyms for Hodgkin's disease. (16) Give morbid anatomy and morbid histology of glands in lymphadenia. (17) What primary tumors occur in lymph-glands? (18) What secondary tumor?

CHAPTER VIII.

ALIMENTARY CANAL.

The **alimentary canal** consists essentially of a tube extending from the lips to the anus, with dilatation at various points for the temporary lodgment of food during the processes of digestion. In the different parts of the canal, we have emptying ducts of glands whose secretions promote digestion. These glands are anatomically distinct from the alimentary canal, but physiologically they are as much a part of the canal as the glands in the mucosa; thus the essential and important secretions of the mouth are supplied by the salivary glands, all of which lie without the mucosa of the oral cavity; the secretion of the stomach is supplied from glands in its own mucosa; the intestinal mucosa supplies a certain amount of secretion, but the preponderance of secretion, utilized in intestinal digestion, comes from the pancreas and liver. As each special area in the alimentary canal is dealing with a material whose chemistry differs from the material in other areas, and as there are important modifications in the anatomy of each area, the diseases of the various areas will also differ.

For convenience in study, the alimentary canal is divided into the mouth (including the pharynx), esophagus, stomach, small intestine, and large intestine.

THE MOUTH.

The mucous membrane of the mouth consists of a thick layer of stratified epithelium resting upon a loose and elastic basement membrane, under which we have a most abundant

submucosa containing a large quantity of loose connective tissue; this is necessary in order to enable the mucous membrane to adapt itself to the sudden changes in volume which the mouth is constantly undergoing.

Malformations of the Mouth.—The mouth being developed from four branchial arches, failure of any of these to unite results in the formation of clefts, which, at birth, constitute some form of **harelip** or some analogous condition. Where the failure of union is restricted entirely to the upper lip and invades the soft parts only, the condition is harelip, pure and simple; where, however, the hard palate is also involved, the resulting condition is known as **cleft palate.** The fissure may be limited to a small niche between the incisors and canine teeth, or it may extend entirely through the hard plate, converting the nasal and oral space into one cavity; occasionally the failure of union extends still further—a cleft palate becomes **cleft face.**

More or less faulty development of the arch which forms the inferior maxilla may result in a cleft at the chin or entire absence of the bone—a condition known as **agnathia.** Agnathia is likely to be associated with cyclopia. Arrests in development may give rise to fistulæ, through which the mouth, or pharynx, may communicate with the external surface by some abnormal route.

Tongue-tie (*ankyloglossia*) consists of a shortened condition of the frenum of the tongue.

Inflammation of the mouth is known as **stomatitis,** and may be catarrhal, pseudomembranous, gangrenous, hemorrhagic, or suppurative. (For morbid anatomy, morbid histology, etc., of these, see "Inflammations of Mucous Membranes," p. 448.)

Follicular stomatitis is an inflammatory process in which the follicles or mucous glands are the seat of the most active inflammation with the development of vesicles, closure, and

finally distention of the ducts which may terminate in coagulation necrosis of the upper layer, giving rise to small ulcers.

Ulcerative stomatitis, also known as *putrid sore mouth,* occurs in weak, debilitated children, and occasionally in adults; improper feeding and failure to keep the mouth clean may cause it; chronic poisoning, such as lead, mercury, or phosphorus may induce this condition. It occasionally shows a disposition to be contagious, and this suggests the possibility of its being due to a specific germ, which, however, has not been demonstrated.

It usually begins as an ulcerative process around the teeth, which may become affected and drop out. The ulcers extend along the gum, rarely involving the tongue and cheek; the base of the ulcers contains a grayish-white slough; the accompanying catarrhal inflammation, with decomposition of the inflammatory products and necrotic tissue, gives rise to an exceedingly disagreeable, sickening stench, which has given the disease the name of **putrid,** or **fetid, stomatitis.**

Parasitic stomatitis, or *thrush,* is an infection which occurs most frequently in nursing children, and is due to the *Saccharomyces albicans.* (See p. 303.) This fungus does not seem to attack the normal mucous membrane, but becomes engrafted upon a mucosa which has its surface eroded or irritated by improper feeding or other causes; the disease is occasionally seen in adults after, or during, acute febrile processes or chronic diseases. The parasite pullulates in the interstices of the epithelium and forms a membrane, usually superficial, but which may extend to the basement membrane and, by mixed infection, may lead to ulceration. The disease usually begins on the tongue, but may arise primarily on, or spread to, the cheek, and thence to the tonsils, palate, pharynx, and esophagus; it differs from the preceding forms of stomatitis in the presence of the germ and in the fact that

it is usually associated with marked dryness of the mouth, in contradistinction to the ptyalism which accompanies other forms.

Gangrenous stomatitis, also known as *cancrum oris* and *noma*, usually begins as a gangrenous process, attacking the gums or cheeks, attended by sloughing in the structures involved. The soft parts and bones may become gangrenous and slough, so much so that a greater part of the face may be destroyed by the phagedenic process. The disease usually follows some of the acute infectious processes in children; Osler states that 50 per cent. of the cases follow measles. Girls suffer more frequently than boys. The disease is most frequent between the second and fifth year; the cases which the writer has seen have been in older children—seven to nine. The disease usually terminates fatally by septicemic processes. The constancy of the lesion, as well as its characteristics, indicate that the disease is probably mycotic. Lingard has described a thread-like bacillus found in these cases, but not yet fully demonstrated to be the cause.

Diphtheria usually manifests itself in the pharynx. The inflammations which result from infection by the bacillus of diphtheria may be catarrhal, pseudomembranous, or gangrenous; in rare cases all three forms may be present in the pharynx, tonsils, or palate. The process may extend upward into the nasal cavities, forward into the mouth, downward into the larynx, or, in rare cases, into the esophagus.

Catarrhal, *pseudomembranous*, *gangrenous*, or *suppurative* processes may arise in the tonsils, palate, or pharynx, as the result of infection by streptococci. From streptococcus infection of the mucosa there may arise a wide-spread cellulitis of the adjacent structures; when this extends into the neck it is known as *Ludwig's angina*. Suppuration around the pharynx, when diffuse, is spoken of as *phlegmon of the*

pharynx, or, when circumscribed upon the posterior wall of the pharynx, it is known as *retropharyngeal abscess.*

In the tonsils inflammations are likely to be follicular, associated with occlusion of the ducts, and the accumulation of inflammatory products within the follicles, which eventually break down; catarrhal processes of the surrounding mucosa accompany the follicular lesions. Chronic inflammation of the tonsils is also recognized, and is associated with hypertrophy of both the lymphoid elements and the stroma; new gland structure may be produced.

Of the *chronic infections* which may attack the mouth and pharynx, syphilis, tuberculosis, leprosy, glanders, actinomycosis, and rhinoscleroma occur. (For pathology of these see part II, p. 219.)

Tumors of the Mouth and Pharynx.—Of the adult epithelial type, *papillomata* occur on the tongue and cheek, rarely in the posterior part of the mouth or in the pharynx; *adenomata* occur in the tonsil and occasionally in the pharyngeal wall. Of the embryonic epithelial tumors the *squamous epithelioma* is the most common; its usual seat is upon the tongue or lips, more commonly the latter; squamous epithelioma of the lip is, of all forms of cancer, the most frequent. Of the adult connective-tissue tumors, *lipomata*, *fibromata*, *myomata*, *chondromata*, *angiomata*, and *lymphangiomata* occur. The last of these occur as *macrocheilia*, or lymph lip, and *macroglossia*, or lymph tongue; these conditions are sometimes spoken of as *lymphangiectasis*, or dilatation of the lymphatics in the tongue and lip respectively. Of the *sarcomata*, or embryonic connective-tissue tumors, but few occur in the mouth; myeloid sarcoma of the lower jaw is the most common form. Next to these we have *sarcomatous epuli*, which are sarcomata occurring upon the gum and probably in the alveolar process. In the pharynx, *retropharyngeal sarcoma* is one of the recognized tumors.

SALIVARY GLANDS.

Parotitis, or mumps, is an infectious inflammation occurring in the parotid gland. It is, no doubt, due to some form of infection, although exactly what the infectious agent is has not been demonstrated. A chronic infection may occur in any of the salivary glands. The parotid seems more or less susceptible to septic influences, and is not infrequently inflamed during septic diseases, and occasionally in ordinary febrile processes; the condition is referred to as *parotid bubo.*

Hypersecretion, or ptyalism, is occasionally noted in inflammations of the mouth, as a result of chronic poisoning by mercury, phosphorus, or copper, and as a physiologic result of the administrations of jaborandi and certain iodin compounds; it is also present in hydrophobia. The reverse of the preceding—dry mouth, *xerostomia*—has been observed; the exact cause, however, is not known.

Salivary calculi occasionally form in the salivary ducts, and may, by inducing inflammation and suppuration, perforate the cheek and form a new tract, which is, of course, a fistula. These calculi are usually composed of the carbonate and phosphate of lime, and are rarely large or very firm.

Obstruction to the duct of a salivary gland gives rise to a retention cyst known as a **ranula**; these are usually named after the gland involved, as *ranula submaxillaris*, *ranula retromaxillaris*, and *ranula sublingualis.* The classic ranula, so long considered a cyst of the duct of Wharton, is now believed to be a mucous cyst in the Blandin-Nuhn gland.

Tumors of the salivary glands are not common. Of the adult epithelial type, *adenomata* occasionally occur; they are, however, exceedingly rare. Of the embryonic epithelial-tissue tumors or cancers, *epitheliomata* are the most frequent, and these, histologically, are usually of the tubular variety, although squamous epithelioma has been observed. *Encepha-*

loid and *scirrhus* are rare. Of the adult connective-tissue tumors, *chondromata*, *fibromata*, and *myomata* occasionally occur; perhaps the most frequent tumor of the salivary glands is the fibro-adenoma of the parotid. It is not, however, a common growth. Other connective-tissue neoplasms have been observed. Of the embryonic connective-tissue tumors, *sarcomata* occasionally occur.

ESOPHAGUS.

Normal Structure.—From the pharynx to the anus the essential structure of the musculomembranous tube, the alimentary canal, is a mucous membrane resting upon a muscular wall composed of two or more layers of unstriped muscular fiber. The variations at different points usually consist in different glandular and epithelial layers, but the esophagus differs also in its muscular layer from the remainder of the tube, in that the upper part has little or no unstriated muscle, while the lower end is, like the remainder of the alimentary canal, made up exclusively of unstriped muscular tissue. The epithelium of the esophagus is stratified throughout.

Malformations.—Very rarely the organ may be absent. Rarely, from faulty union of clefts, there may be *fistulæ*. *Diverticula*, or the reverse, *stenoses*, are occasionally found.

Inflammations.—*Esophagitis* usually results from injury. The catarrhal form may arise by extension from the contiguous mucosa above. Pseudomembranous and gangrenous inflammations are extremely rare. The thick epithelial layers render the infections less frequent than one might expect. *Thrush* of the esophagus has been observed, and is usually secondary to a similar process in the mouth. *Peri-esophageal suppuration* occurs as the result of injury, diseases of adjacent structures, and pyemia. *Syphilis* is the most frequent chronic infection, and usually manifests itself as a gummatous or fibroid change, leading to stricture.

Catarrhal, hemorrhagic, and *gangrenous* processes follow the application of corrosive substances, as strong acids, alkalies, and cauterants, mercury, salts of copper, etc.; scalds and burns induce similar changes. The severity of the process varies, and depends upon the agent used, the concentration, the length of time which it acts, and the age of the patient. The young, tender mucous surfaces are specially prone to suffer. Ulceration may follow, should the patient survive, and contraction of the healed ulcers may cause stenosis. It is remarkable that pseudomembranous inflammations so rarely attack the esophagus.

Acquired stenosis of the esophagus occurs in two forms:

(1) **Esophagismus** (*spasmodic, hysteric*, or *non-organic, stricture*) arises as (*a*) a manifestation of hysteria, or as (*b*) a reflex phenomenon due to excessive irritability. A tender point in the esophagus—a minute abrasion or ulcer—is so sensitive that as soon as touched by a bolus of food, or an instrument used for exploration, spasm ensues, and only relaxes after considerable force is continuously applied for some time.

(2) **Organic stricture of the esophagus** is a narrowing of the tube, independent of muscular contraction, and due to disease. The narrowing may be a single annular band or the stricture may be several inches in length. There are two places in the esophagus where strictures are most frequent: the upper area of election is just behind the cricoid cartilage; the lower, opposite the bifurcation of the trachea.

Causes.—Cicatrization following injury, as that of burns, scalds, or escharotics; contraction and occlusion incident to the growth of cancer; syphilis.

Stricture of the esophagus gives rise to **esophageal obstruction**, for which there are many other causes—*e. g.*, foreign bodies lodged or wedged in some part of the tube; polypoid tumors of the esophagus (rare); pressure on the esophagus from tumors of surrounding structures, as medias-

tinal sarcoma, aneurysm of aorta, swollen lymph-glands, tuberculosis, or other disease, of the vertebræ. Pressure obstruction may occur at any point; the points of stricture obstruction have been indicated.

Acquired dilatation of the esophagus is always secondary to some other process. It has been known to follow spasmodic stricture. Organic stricture, or any form of obstruction, is likely to lead to dilatation above the point of narrowing. The sac may be fusiform, globular, or, in rare cases, may extend in one direction, forming a diverticulum. A form of dilatation occurring without obstruction, and supposed to be due to atony of the pharyngeal muscles, has been described; the sac in such cases is fusiform. Diverticula, or localized saccular dilatations, occur as the result of lesions in the submucosa, softening that structure and the muscular wall; the mucosa is then, by internal pressure, forced through the point of softening. Such diverticula occur in the lower part of the pharynx, and are spoken of as **pharyngoceles.** Small, funnel-like diverticula are occasionally noted in the lower part of the esophagus, near the bifurcation of the trachea, and on the anterior surface. These are due to traction by adherent cicatrices.

Perforation of the esophageal wall may result from within outward in ulcerative processes, as in cancer, ulceration following injury and lodged foreign bodies. Extensive laceration, with infection of the esophagus by a bougie, is not so rare as it should be. Perforation from without may result from wounds, peri-esophageal suppurative processes, and pressure, as in tumors, aneurysm, goiter.

Tumors of the Esophagus.—Adult epithelium: *Papilloma* occurs, but *adenoma* is very rare. Embryonic epithelium: *Carcinoma* is the most frequent tumor of the esophagus. The form most frequently noted is the *squamous epithelioma*, although all forms of cancer may invade the esophagus.

All forms of connective-tissue neoplasms are rare, although

of the adult type *fibromata*, *myxomata*, *lipomata*, and *myomata* occur. *Sarcoma*, as a primary growth, is rare, but few cases have been reported; where sarcoma reaches the esophagus, it is usually by extension from contiguous tissues.

STOMACH.

Normal Structure.—(1) External or serous coat. (2) Middle or muscular coat, made up of three layers of unstriped muscular fiber; the outer layer is the longitudinal layer; the inner layer is arranged obliquely, while the circular fibers are between the oblique and longitudinal layers. The circular fibers are most abundant near the pylorus. (3) *The mucosa*—The muscular and serous layers are elastic, while the mucosa is less so, as a result of which it lies in folds and elevations when the organ is empty. The submucosa is abundant and loosely woven. The epithelium of the stomach is cylindric, but as it enters the ducts of the glands it becomes shorter and eventually cuboid. The glands are of two kinds, one predominating at the cardiac end, in structure both simple and branched, and containing columnar, cuboid, ovoid, and central cells; the other glands, predominating at the pylorus, are also simple and branched, but differ from the preceding in that the neck or duct is longer and the ovoid or parietal cells are absent.

During life the mucosa is pink, occasionally red, but postmortem it assumes a much darker hue; this is most marked in the dependent portion, and may be mistaken for evidence of disease or injury. Immediately after death, gastric digestion continuing, more or less destruction of the wall of the stomach may result. The mucosa, which has undergone partial or complete digestion, is converted into a soft, pultaceous, transparent, or blackish pulp. The process is most marked in the dependent portion, and may extend through the gastric wall and involve the adjacent structures, even perforating the diaphragm.

Malposition and Malformation of the Stomach.—In the *situs inversus*, and in fissural malformations of the abdominal wall or diaphragm, the stomach may be transposed, or, in the latter instance, be forced through the fissure and become more or less extra-abdominal. *Stenosis of the pylorus*, or even complete *atresia*, may occur. *Sacs*, *abnormal septa*, and *circular constrictions* have been found.

Hyperemia of the stomach is a physiologic process during digestion, and also occurs during the initial stage of acute inflammations.

Congestion of the stomach is most marked in cardiac and pulmonary diseases associated with venous stasis. An intense congestion has been mistaken for the lesions of a destructive or escharotic poison.

Hemorrhage from the stomach, or **hematemesis.**

Causes.—Vomiting of blood may be the result of congestion, whether due to portal obstruction, as in cirrhosis of the liver, or cardiac disease. In the intense hyperemia of acute inflammations and the vascular distention of severe chills, as in malaria, hematemesis is occasionally seen. Trauma, cancer, ulcer, poisons, and severe retching, as in the vomiting which accompanies poisoning, may induce the hemorrhage. It may be vicarious. Constitutional diseases and specific infections, such as small-pox, yellow fever, purpura, and profound anemia are, in rare cases, complicated by hematemesis. Aneurysm of the aorta may rupture into the stomach. Blood may be vomited which originally came from some other structure, as the blood swallowed during operations on the mouth, also in hemoptysis, epistaxis, and esophageal hemorrhage; in nursing babies the blood may have been sucked from the mother's breast. Aneurysm and varicosity of the gastric vessels occasionally act as causes. Rarely, no cause can be demonstrated.

Morbid Anatomy.—The blood is usually clotted, has not the red, frothy appearance of the blood of hemoptysis, is acid in

reaction, and may show partial digestion; that is, be black, greenish, or "coffee ground." Postmortem, many of the lesions may be evident,—as cancer,—but often a most careful search will have to be made for minute ulcers or small ruptured aneurysms. There may be no blood in the stomach, but tarry material may be present in the intestine.

Gastritis (*inflammation of the stomach*) may be catarrhal, either acute or chronic, pseudomembranous, hemorrhagic, or gangrenous. Suppurative processes in the gastric wall are rare, and occur as submucous abscesses or a diffuse interstitial suppuration in pyemia and allied conditions.

Tuberculosis and *syphilis* occur, but are very rare. (For pathology of inflammations of the mucosa see part III, chap. IV, p. 448.)

Mycoses of the stomach occur as (1) infections of the contents by non-pathogenic bacteria, such as the sarcinæ and yeasts, and as (2) infections of the wall (*mural implantation*), such as thrush, diphtheria, and anthrax.

Neuroses of the stomach include those manifestations not associated with any organic or structural lesion demonstrable: certain forms of gastralgia, hysteric manifestations, rumination or merycism, etc.

Gastric dilatation, or **gastrectasis,** or *dilatation of the stomach*, occurs in two forms: (1) *Acute*, due to gorging or overdistending the stomach, and (2) *chronic* dilatation. The latter results from (*a*) obstruction at the pylorus, (*b*) atrophy, relaxation, or atony of the muscular wall. In the first group the stomach wall may be thickened as the result of the resistance which must be overcome in order to expel the gastric contents—a compensatory hypertrophy of the muscular coat. In the second group the wall is thin and the mucosa usually atrophied; the cause is here to be found in repeated overfeedings, catarrhal conditions, and general wasting diseases.

Pyloric obstruction may result from healing of ulcers and

contraction, from fibroid thickening, cancerous processes, rarely adenoid deposits, pressure from without—*e. g.*, cicatricial bands, tumors, as cancer of the pancreas, and from floating kidney. Obstruction may be congenital, or, rarely, foreign bodies may induce it.

Peptic ulceration, perforating gastric ulcer, *simple ulcer of the stomach*, or *round ulcer*, is here described, although an identical process occurs in the duodenum and a closely-allied condition in the esophagus.

Causes.—Embolism or autochthonous thrombosis; inflammations of the mucosa, more particularly the hemorrhagic and gangrenous inflammations; injury (?); congestion, such as accompanies cirrhosis of the liver and chronic heart disease. Predisposing to ulceration are profound anemia, any systemic condition which greatly lowers the body nutrition, and hyperacidity of the gastric secretion. Burns and scalds of the skin have been assumed to be both predisposing and exciting factors in the production of duodenal ulcer. The ulcer is more frequent in females than in males, and is rare, although not unknown, during infancy and childhood.

Morbid Anatomy.—Commonly it is single, but as many as 34 have been reported as being present at one time. In the stomach, peptic ulcers are usually near the pylorus, on the posterior wall, close to the lesser curvature. They vary much in size, are usually funnel-shape, although they may have deeply undermined edges. They not uncommonly implicate large vessels, and violent hemorrhage may, therefore, accompany them. The edges are usually smooth and regular, but may be terraced, thickened, or indurated, and, rarely, serpentine. The floor of the ulcer may be smooth, present the normal structure of the exposed tissue, muscle, or peritoneum, or evidences of attempted healing may be shown in poorly-developed flabby granulations; the floor of the ulcer may be a part of an adjoining organ, the gastric wall having entirely disap-

peared; by such attachment perforation into the intestine or colon may occur, or, rarely, communication with the surface or the thoracic cavity may take place. Perforation into the peritoneum is not uncommon. Should healing occur, a puckered cicatrix results; and if near the pylorus, stenosis may ensue.

Tumors of the Stomach.—Adult epithelium: *Papilloma* and *adenoma* occur, but are rare. The malignant adenoma of the German writers is truly a form of carcinoma. Embryonic epithelial tumors or cancers of the stomach are the most frequent tumors. They usually occur at the pylorus, but there is no part of the stomach exempt. In rare cases they are secondary. The majority of the growths are *cylindric-cell epitheliomata;* next in frequency occur *encephaloid*, *scirrhus*, and *colloid*, in the order given. Metastasis occurs in nearly all cases. Of the adult connective-tissue tumors, but few occur; *fibromata*, *myomata*, and *lipomata* have been observed. Embryonic connective-tissue tumors—*sarcomata*—are rare.

INTESTINE.

Normal Structure.—The intestine is lined throughout by a single layer of cylindric cells; the submucosa is abundant and richly vascular. Situated in the mucous membrane of the small intestine we have small, isolated areas of lymph-adenoid tissue, constituting what are known as solitary glands; where these are agminated, the resulting masses are known as the patches of Peyer. For increasing the absorbing surface of the mucous membrane, it is thrown into villi and folds; these also increase its liability to injury and disease.

Malformation and Malpositions.—These may be congenital or acquired; of the congenital narrowing, or **stenosis,** imperforate areas, or **atresia,** occur; the latter are most commonly situated near the anus. The canal may be abnormally long or the reverse; occasionally a diverticulum situated about one meter above the ileocecal valve is found; this is

known as *Meckel's diverticulum*, and is due to the faulty closure of the omphalomesenteric duct; this may remain as a blind pouch or may open externally at the umbilicus. In fissural deformities of the abdominal wall the intestine may be extruded, causing a form of prolapse. Of the acquired deformities and displacement strictures due to disease, twisting of the bowel, knotting of the bowel, and hernia occur.

Obstruction of the bowel may result from the contraction of any inflammatory exudate which encompasses the organ; malignant disease, most commonly scirrhus, although other forms of cancer and even sarcoma may cause obstruction. Obstruction may also arise from malformations and malpositions, twisting of the bowel or volvulus, tumors of neighboring organs pressing on the bowel, foreign bodies in the bowel, accumulations of fecal matter, and intussusception. In the latter condition a portion of the intestine is invaginated within a part below; the intussusception is always from above downward; as to site, it is most common at the ileocecal valve, but occurs also in the ileum, colon, and in the rectum. As soon as intussusception occurs, the part of the bowel invaginated has its circulation interfered with, and this is followed by infection; inflammation ensues, and, in favorable cases of unrelieved intussusception, the invaginated portion sloughs and may be passed with the stools, and recovery occur; repair takes place by the throwing out of fibrinous material and the adhesion of the two serous surfaces at the point where the invagination begins. Should this adhesion not be perfect, perforation and infection of the abdominal cavity take place. If the adhesion is perfect, a fibrous cicatrix forms, which, as organization and contraction ensue, may give rise to a stricture.

Dilatation of the bowel may result from anything which occludes the passage and favors occlusion; atony of the muscle is a cause; chronic constipation also acts as a cause. Gradually developing obstruction or stenosis may give rise to

dilatation. The colon may be extremely capacious, especially in chronic obstruction. If the obstruction is due to atony of the bowel, the dilated wall will be thin; if the cause is gradually developed, as from a slowly contracting stricture or a malignant growth, the wall will probably be thick, as the muscular layer may have hypertrophied in an attempt to overcome the progressively increasing obstruction.

Inflammation of the intestine may be catarrhal, pseudomembranous, gangrenous, hemorrhagic, suppurative, or chronic infectious. Pathologically, there is little difference between the lesions of different parts of the intestine in any given inflammatory process. The catarrhal inflammations present the same morbid conditions in different parts, but may give rise to peculiar complications owing to anatomic differences—*e. g.*, catarrhal duodenitis may extend to the bile duct; catarrhal appendicitis may produce obstruction of the appendix, where it empties into the colon, by swelling the submucosa at the narrow point of communication between the two viscera. At times the follicles are particularly the seat of the inflammation, and gangrenous processes may give rise to follicular ulcers, or the lymphoid elements which make up a Peyer's patch may be particularly involved. Again, the exudate may be very abundant, as is observed in the severe serous diarrheas; occasionally the reverse may be the case. The above inflammations in the various parts of the intestine are as follows: Duodenum, duodenitis; jejunum, jejunitis; ileum, ileitis; appendix, appendicitis; head of the colon, typhlitis; colon, colitis; rectum, proctitis.

As previously stated, the pathology of these processes does not differ in any essential manner from that observed on other mucous membranes, for description of which see chapter IV, part III, page 448.

Dysentery occurs as a catarrhal, gangrenous, hemorrhagic, or suppurative inflammation of the colon, although the small

intestine may be involved in the morbid process. When due to the Amœba coli, irregular, indurated ulcers develop in the colon; these may undermine and coalesce in the submucosa; the undermining is less marked, usually absent, in gangrenous or diphtheric dysentery. In chronic dysentery, cicatrices form, ulcers redevelop from time to time, and all possible combinations of inflammatory phenomena may occur. In all forms of dysentery septic and pyemic lesions may arise.

Infectious Processes.—**Cholera,** due to the spirillum of Asiatic cholera, is attended by a most violent serous catarrhal inflammation of the mucous surface. In the latter stages follicular involvement may be marked, and ulceration may occur.

Typhoid or Enteric Fever.—More or less marked catarrhal inflammation, with a varying serous and desquamative element, accompany the other intestinal lesions. Early in the disease the follicles become swollen and prominent, hyperemic, and occupied by proliferated cell elements; rarely the process is sufficiently intense to cause necrosis and ulceration of the solitary follicles. In the agminated follicles, the patches of Peyer, the hyperemic swelling and the cell proliferation are more marked, and the bacillary infiltration deeper. The patches are elevated, edematous, and surrounded by a slight zone of redness; at first the patch is intensely engorged and deeply colored, but later the circulation is arrested, necrosis occurs, the slough is thrown off, and an ulcer results. The depth of the ulcer is dependent upon the extent of the necrosis; it may involve only a part of the mucosa, but more commonly the entire thickness of the mucous membrane is destroyed and the submucosa or muscularis exposed. The edge of the ulcer is irregular, swollen, and, it may be, undermined. The base of the ulcer, after the slough has completely disappeared, is clean and smooth. If the sloughing process be attended by vascular stasis in the muscularis, the slough may perforate, or

perforation may occur after the slough has been thrown off. If a vessel of any size be opened in the process of sloughing, or if there be no coagulum formed in an open vessel, hemorrhage results. With separation of the slough, in favorable cases, repair begins; embryonic, then granulation, tissue develops, and epithelial reproduction proceeds from the margins toward the center.

The typhoid ulcer is oval in outline, with its long diameter in the axis of the bowel; it rarely involves the entire patch, but may do so; the ulcers are most abundant, and most constant, near the ileocecal valve, but may develop in any part of

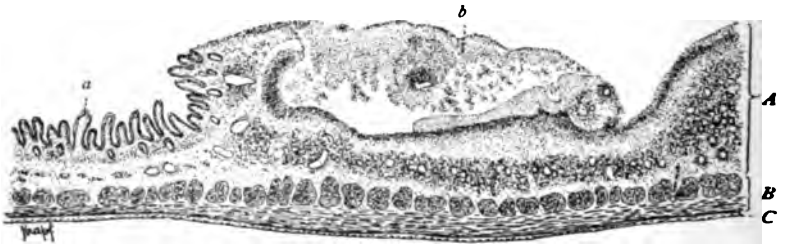

FIG. 253.—SECTION THROUGH A TYPHOID ULCER, END OF SECOND WEEK OF THE DISEASE.—(*Schmaus.*) (PARTLY DIAGRAMMATIC.)

A. Mucosa and submucosa, the latter infiltrated with small round-cells. *B*. Muscular coats of intestine. *C*. Serous layer of intestine. *a*. Adjacent nearly normal mucosa. *b*. Separating slough.

the intestine where the lymphoid elements are present. Chronologically, infiltration and cell proliferation terminate in necrosis about the last of the second week or in the beginning of the third week; during the latter the sloughs separate; healing may not be completed until clinical recovery has been long passed.

With infiltration of the Peyer's patch, and the generation of poisons therein, the lymphatics and blood-vessels begin the absorption of toxins, whose influence may be wide-spread; at the same time the bacilli gain access to the viscera and may be found, not only in the patches, but in the mesenteric glands,

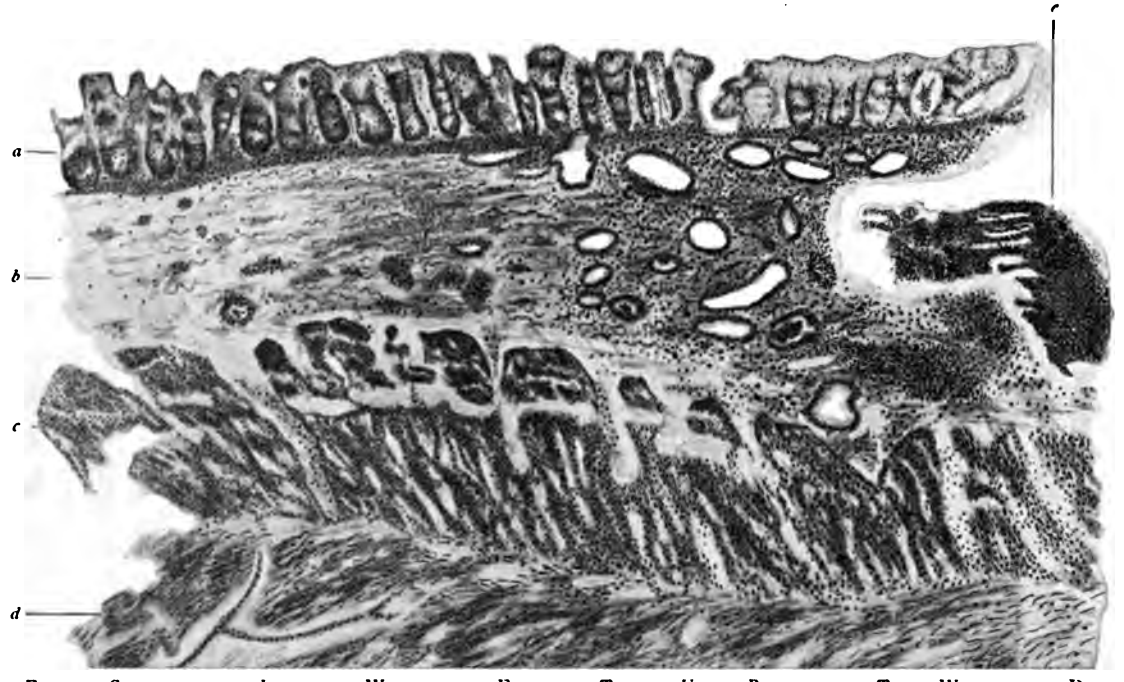

FIG. 254.—SECTION OF THE INTESTINAL WALL AT THE EDGE OF A TYPHOID ULCER, BEGINNING OF THIRD WEEK OF THE DISEASE. MUCH HIGHER MAGNIFICATION THAN FIGURE 253. (¼-inch objective, ½-inch projection ocular.)

Specimen hardened in corrosive sublimate, infiltrated with paraffin, stained in hematoxylin and eosin, and mounted in balsam. *a*. Mucosa, which overhangs the margin of the ulcer. *b*. Submucosa, infiltrated with serum and containing some fibrin. Near the ulcer well-marked and extensive round-cell infiltration is seen. *c*. Transverse muscular fibers; immediately under the ulcer these will be seen to contain many round-cells and show degenerative changes not discernible with this magnification. *d*. Longitudinal muscular fibers. *e*. Slough of necrotic tissue matted together, and about separated, preliminary to being thrown off.

spleen, liver, and, although rarely, in the blood. The mesenteric glands are infiltrated, and may be necrotic; suppuration due to the pyogenic activity of the bacillus, or to mixed infection by pyogenic cocci, may occur. The adjacent lymphatic glands (retroperitoneal) may be involved.

The spleen is enlarged, soft, and may show infarction, rupture, or gangrene.

The liver shows cloudy swelling, and may contain areas of coagulation necrosis.

The kidneys exhibit a similar change, or may even pass into acute nephritis.

The muscles of the abdomen and the adductors of the thighs may show hyaline or vitreous degeneration. Rarely, other muscles may be involved. Granular change or cloudy swelling may be present in the cardiac muscle. Inflammatory or even suppurative processes may occur in other organs—*e. g.*, parotid glands, in the bones, etc. The cause of these is not always apparent, but may be due to embolism, to infection by typhoid bacilli, or other bacteria gaining ingress through the open ulcers in the intestine. Infective processes may occur in the portal vein.

Syphilis of the intestine is rare; it usually occurs in the rectum, where a firm fibroid stricture may develop from gummata deposited around the bowel. The stricture develops slowly, is most common in women, and may or may not be attended by ulceration; most commonly this is absent. (For description of syphilis of mucosæ, see p. 464.)

Tuberculosis of the intestine may occur as a primary or secondary process; it may be miliary without ulceration, or, more commonly, ulcers develop. The tubercles are commonly developed in the adenoid structures; caseation follows; this destroys the overlying mucosa and an ulcer results. The ulcer, if of any size, is irregular, its long axis transverse to that of the bowel, its edges infiltrated and caseous, and, if

examined by transmitted light, tubercles may often be seen in its base. The serous surface is puckered from newly-developed fibrous tissue; if the ulcer passes around the bowel, a stricture may be developed; tubercles may be seen in the peritoneal covering of the intestine; the lymphatic glands are likely to be involved. (For description of tuberculosis of mucous membranes, see p. 462; also Fig. 245, p. 463.)

Tubercular abscesses in and around the rectum may give rise to *fistulæ*, which may communicate internally with the bowel,

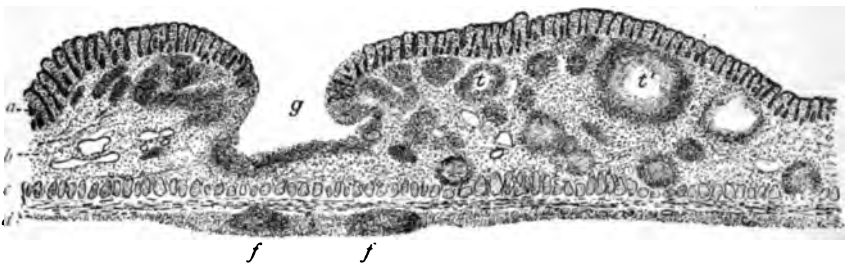

FIG. 255.—TUBERCULAR ULCER.—(*Schmaus.*) × 12 diameters.

a. Mucosa. *b*. Submucosa, in which are numerous tubercles. *t* and *t'*. In the latter, caseation is advanced. *c*. Muscularis. *d*. Serous covering, in which, at *f*, *f*, are two tubercles. *g*. Opening of ulcer into the lumen of the canal.

or externally through the skin, or with both the bowel and cutaneous surface.

Leprous nodules and ulcers occur in the colon, rarely in the small intestine.

Actinomycosis occurs in the intestine, both large and

Tumors of the Intestine.—Of the adult epithel
adenomata occur; these may, occasionally, be
although they are commonly sessile; they ar
in the rectum, and are extremely likely
Papilloma occurs about the anus, bu
epithelial tumors are most common
they are usually cylindric-cell e
forms of cancer, including scir

mous epithelioma occurs in the lower part of the rectum near the anus. Of the connective-tissue tumors, *fibromata* and *myomata* are the most frequent, although rare. *Sarcomata* occasionally invade the intestine.

Varicosities of the veins of the rectum, particularly the hemorrhoidal veins, constitute what are known as *hemorrhoids*.

QUESTIONS.

(1) What malformations may occur in the mouth and pharynx? (2) What is harelip? (3) What is cleft palate? (4) What is agnathia? (5) What diseases may occur in the mouth and pharynx? (6) What inflammatory processes may occur in the mouth and pharynx? (7) Give pathology of ulcerative stomatitis. (8) Give causes and pathology of parasitic stomatitis. (9) Give pathology and synonyms of gangrenous stomatitis. (10) What morbid conditions may arise in the throat as a result of infection by the bacillus of diphtheria? (11) What inflammatory processes may follow streptococcus infection? (12) What morbid conditions may occur in the tonsils? (13) What tumors occur in the mouth and pharynx? (14) What is (*a*) macrocheilia? (*b*) macroglossia? (*c*) lymphangiectasis? (15) What diseases may occur in the salivary glands? (16) What is parotitis? (17) What is parotid bubo? (18) What is ptyalism? (19) What is xerostomia? (20) Give composition and results of salivary calculi? (21) What is a ranula? give the different forms. (22) What tumors may occur in the salivary glands? (23) Give malformations and diseases of the esophagus. (24) Give forms of ...phagitis. (25) How may syphilis affect the esophagus? (26) What slow ...litions follow the application of cauterants, scalds, burns, and other attendes? (27) What are the forms of esophageal stenosis? give descriptio. (28) What are the forms of esophageal dilatation? give

Tubercul...) What is a pharyngocele? (30) How may perforation of the ...ur? (31) What tumors may occur in the esophagus? (32) secondary proce...al color, and what are the postmortem changes usually more commonly, ...h? (33) What malpositions and malformations may developed in the aden... (34) Under what conditions may gastric hyperdestroys the overlying ...r? (35) Give causes of hematemesis. (36) ...s may occur in the stomach? (37) To what ulcer, if of any size, is irre... (38) What is meant by a gastric neuthat of the bowel, its edges ... and causes of gastric dilatation? ...on. (41) Give causes and morbid

anatomy of peptic ulcer. (42) To what tumors is the stomach liable? (43) What diseases may occur in the stomach? (44) Mention the malformations and malpositions which may occur in the intestines. (45) Give causes of intestinal obstruction, and describe intussusception. (46) Give causes of dilatation of the bowel. (47) What inflammatory processes may occur in the bowel? name the inflammatory processes in each anatomic division. (48) What are the causes and forms of dysentery? (49) What morbid processes accompany cholera? (50) Give morbid anatomy of typhoid fever. (51) Differentiate a tubercular from a typhoid ulcer. (52) What chronic infections occur in the bowel? (53) What tumors occur in the bowel? (54) What is a hemorrhoid?

CHAPTER IX.

LIVER.

Normal Structure and Function.—Essentially, the liver is a mucous membrane in which the connective tissue which passes throughout the organ is the basement membrane, and the cell elements of the lobules are the epithelial cells upon which the functional activity of the organ depends. The lobules are formed of hepatic cells arranged in radiating rows from a common center. The vascular supply passes from the periphery of the lobule toward the center, and the biliary capillaries pass in the opposite direction. The lobule is the gland unit and the hepatic cell the cell unit. The gland differs from all other glands in its blood supply; there is the usual arterial supply represented in the hepatic artery; to this is added the portal supply—an enormous volume of blood, brought from the digestive canal, laden with the products of food metabolism. The portal vein is distributed to the periphery of the lobule, and the zone immediately adjacent is known as the *portal vein zone;* in the center of the lobule is the hepatic vein, which drains the blood from the lobule, and the tissue immediately surrounding this is known as the *hepatic vein zone;* between the two areas, just indicated, lies a zone known as the intermediate or *hepatic artery zone.* Histologically and physiologically, these zones are not differentiated; but disease processes, as we will see later, outline them in a more or less well-marked manner.

The lobule is surrounded by connective [illegible] which is continuous with that of the median fissure [illegible] is known as the capsule of Glisson; in

hepatic artery, and the bile ducts ramify, and these carry into the lobule sufficient of the connective tissue for support. In man, the lobule is not sharply differentiated, and many lobules appear confluent. By confluence or juxtaposition many lobules form a lobe, and these, the organ. The portal vein, representing the collected blood from the alimentary canal and spleen, is of itself a circulation, in the sense that there is a capillary system at either end. It differs from the other blood systems, pulmonary and systemic, in that, between the two capillary areas,—the one in the intestine, stomach, etc., and the other in the liver,—there is no propelling body, and the blood must flow, in this subsidiary circulation, by reason of the cardiac force distributed to the capillary system in which the portal vein finds its origin. Pathologically, this is of the greatest importance, for where the general circulation is feeble, wherever there may be a tendency to stagnation, to venous stasis, how unfortunately situated is the portal system to escape the inevitable result! When the blood leaves the surface, as in the chill of malaria, and there is a tendency to distention of the veins, those of the portal circulation are most prone to suffer. So it is that obstructive diseases of the lung or heart, which impede the onward flow and favor stasis in the veins, evince their most marked phenomena in the hepatic and digestive structures.

Physiologists have agreed that the liver performs the following functions :

(1) *Hematolytic :* Disorganization of blood elements is necessary to the production of bile coloring-matter, and it is generally believed that this hemolysis is, at least partly, carried on in the liver.

(2) *Secretory :* Bile is not only eliminated by the liver, but is manufactured by the hepatic cells.

(3) *Urea production :* The liver is believed to be influential in the production of urea.

(4) *Glycogenic :* Glycogen is manufactured in the liver.

(5) *Antitoxic:* The interception of poisons.

The latter has been demonstrated of strychnin, in which a dose by the stomach or injected into the liver blood supply may be much larger, and less injurious, than similar doses given by the systemic circulation. Toxicologists also recognize the filtering influence of the liver, in that poisons may be recognized in that organ when not discoverable elsewhere.

Malformation and Deformity of the Liver.—Malformation of the liver at birth is not common. Rarely, the liver may be absent. Increase or diminution in the number of the lobes, occasionally occurs; the gall-bladder may be absent, partially developed, or ductless, the duct having been occluded after the formation of the diverticulum which should form the bladder; with absence of the gall-bladder there may be some dilatation of the hepatic duct. Acquired deformities, not due to disease, are the result of pressure—*e. g.*, by tight lacing, the wearing of tight belts, pressure from tumors in adjacent structures, etc.

Malpositions of the liver are rarely congenital; the organ may be transposed, as in the *situs inversus;* laxness of the ligaments may give rise to what is known as the *hepar mobile*, or *floating liver;* occasionally, a liver is found which is so attached by its ligaments as to permit rotation on its transverse axis, at times presenting its edge forward and again its broadest aspect, thus, by altering the area of dulness, misleading the clinician; in the same way a liver may be so suspended as to always present its broad surface, and thereby appear large, or, by always presenting its edge, it may appear small. Acquired malposition may result from pressure from above, as in pleuritic effusion of that side; displacement upward, as in fibroid or cirrhotic right lung, or increased intra-abdominal pressure.

Hyperemia of the liver is physiologic during digestion, and is by some believed to be constant in diabetes.

Congestion of the liver results from any condition which retards the venous circulation and slows the blood in the infe-

rior vena cava; the most frequent causes of this condition are valvular heart disease, especially mitral disease, pulmonary obstruction, as in emphysema, chronic bronchitis, etc. The retarded circulation backs into the thin-walled hepatic veins, which, being most distensible within the lobule, gradually dilate, and, by pressure, lead to atrophy of the adjacent liver cells; the zone around the hepatic vein is first affected, and may, histologically, be made up entirely of dilated branches of the hepatic vein, with complete destruction of those hepatic cells which lie immediately around the central vein. The retarded circulation favors the infiltration of fat, and the margin of the lobule may contain such an excess of fat that it appears distinctly yellow to the naked eye. Macroscopically, the organ is much larger than normal and may attain considerable size; that this is largely a vascular distention is shown by the fact that where, during life, the veins pulsate, the liver may also manifest this phenomenon. The organ is red, hence the name **red atrophy,** and, on section, oozes considerable blood; the lobules can usually be made out, and the dark-red center of each lobule, with its lighter periphery, resembles a transverse section of a nutmeg, and hence the name "*nutmeg liver.*" In some cases there may be considerable increase in the connective tissue. While the organ during life may be much larger than normal, when removed and drained of blood it shrinks and presents a wrinkled capsule and is much lighter than its size would indicate.

Hypertrophy of the liver does not occur, except as a compensatory process. Where one lobe, or one part of a lobe, is destroyed by disease, there is likely to be an increase in the size of other lobes; thus, in atrophy of one lobe, or a part of a lobe, as a result of pressure, or destruction of one lobe by abscess or cyst, if the patient recovers completely, hypertrophy of the remaining liver tissue may occur.

Atrophy of the liver arises from several causes: (1) **Simple**

atrophy of the liver, due to starvation or inanition—*e. g.*, the writer has, in his collection, a liver weighing but 560 gm., taken from a patient who died slowly, from starvation, as the result of cancerous disease of the esophagus. In such cases, associated with general atrophy, the liver may be reduced to one-third of its normal dimensions and weight. The process is probably both simple and numeric, and begins at the periphery, where the evidences are most marked; there is no part of the organ, however, which is not implicated.

Morbid Anatomy.—Such a liver has a sharp margin, and is darker in color than the normal organ; the relation of lobes, one to another, is normal; after removal from the body and when drained of its blood, the capsule is wrinkled, because the remaining liver cells no longer fill it; the gall-bladder frequently projects from three to seven cm. beyond the margin of the liver. The blood supply to the organ is poor in nutrition; the absence of food from the alimentary canal excludes the normal stimulus to secretion, and, as a result of the combined conditions, very little bile is secreted.

Morbid Histology.—The diminution in size of the lobules is extremely marked; the liver cells are small and atrophied; there seems to be as much fibrous tissue as liver structure, but this is probably due, not to an increase of fibrous tissue, but to a diminution of liver tissue.

(2) **Pressure atrophy of the liver** covers a multitude of lesions. Women who lace tightly, by pressing in the margin of the ribs, produce a deep groove or impression in the larger lobe of the liver and may almost completely divide it; the same result is accomplished in men who wear tight belts, as is so frequently done by a certain class of laborers. The liver is very susceptible to pressure, and is, therefore, influenced by tumors in adjacent organs, tumors and accumulations of gall-stones, or accumulated secretory matter in the gall-bladder.

Another form of atrophy from pressure is **red atrophy,**

which has already been discussed; the pressure is exerted in this form of atrophy by the blood dammed back into the liver lobule, thus compressing the cells and leading to their disappearance. (See "Congestion of the Liver," p. 568.)

A certain amount of atrophy accompanies amyloid infiltration, in that the new deposit in the liver interferes, to a certain extent, with the function of the adjacent cells. Cirrhosis of the liver, by compression of the lobules, also leads to atrophy. Obstructed bile ducts give rise to pigmentation and atrophy of some of the cells. In all forms of atrophy of the liver there is likely to be more or less pigmentation of the organ; beside the pigmentation incident to an atrophic lesion, the lesion itself interferes with the production, and may also obstruct the escape, of the bile. (*Acute yellow atrophy*, see p. 575.)

Infiltrations to which the liver is liable are: (1) Fatty infiltration, (2) amyloid infiltration, and (3) pigmentary infiltration.

Fatty infiltration of the liver arises as the result of an abundance of fat, sugar, or alcohol supplied to the liver, in all of which cases the liver acts merely as a storehouse for the temporary deposition of the nutrient element not needed by the system at large; a certain amount of fat is normal, and is essential to the elaboration of perfect bile. Those causes just cited represent nothing but an excess of the normal.

Fatty infiltration of the liver is also found in these diseases where oxidation is in abeyance. As an example of this form we have the fatty infiltration found in consumption, in cachexia, anemia, and allied conditions. The lesion produced by phosphorus-poisoning is held by some to be a fatty infiltration, and by others a fatty degeneration; it is probably a combination of the two processes.

Morbid Anatomy.—The liver of fatty infiltration is enormously increased in size, and represents about the largest liver ordinarily seen in the postmortem room; it is firm, with its margin rounded, its capsule smooth, pale in color, blood-

less, even on section, and on cutting with a moist, clean knife, distinctly greases the blade. While the organ may weigh from

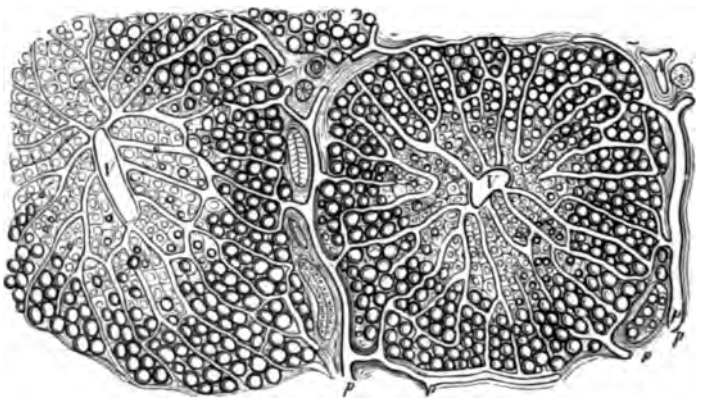

FIG. 256.—FATTY INFILTRATION OF THE LIVER.—(*Rindfleisch.*) (PARTLY DIAGRAMMATIC.)

V, V. Hepatic vein, around which are many normal liver cells. *p, p, p, p, p.* Ramifications of the portal vein which bring the products of digestion directly to the periphery of the liver lobule, into which the fat is infiltrated as large globular collections of oil within the liver cell.

three to four kilos, its specific gravity is low, due to the amount of fat which it contains; the added fat being lighter than water, the organ may have a specific gravity of 1000. The gall-bladder does not extend to the margin of the organ; the bile is usually lighter in color than the normal, but, clinically, there is no evidence, in ordinarily fatty livers, that the bile is deficient in functional activity.

FIG. 257.—FATTY INFILTRATION OF THE LIVER CELLS. —(*Schmaus.*)

Morbid Histology.—In fatty infiltration the fat will be found distributed in the earlier stages, in the periphery of the liver lobule, occupying largely the portal-vein zone; in extremely advanced cases the infiltrated area may approach the center of the lobule, but not until the margin is

extensively invaded. The fat exists, usually, as a single large globule in the liver cell, crowding the nucleus to one side; the latter is usually apparently normal in structure and stain reaction. Liver cells adjoining those containing large quantities of oil are usually normal; there is not likely to be any granular or cloudy change in the unaffected cells, thus differentiating the liver cell of fatty infiltration from the liver cell of fatty degeneration.

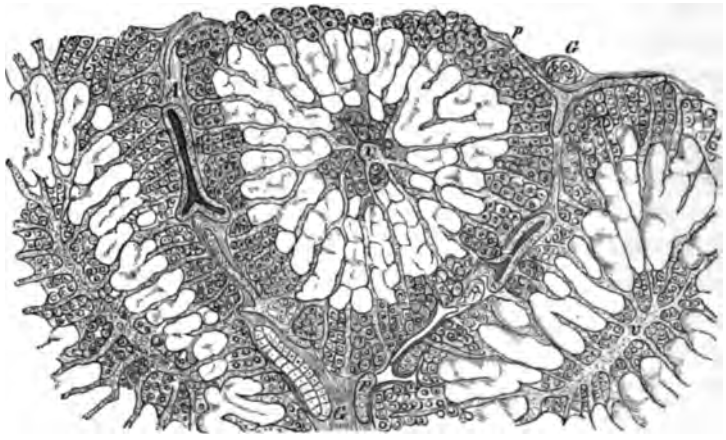

FIG. 258.—LIVER, AMYLOID INFILTRATION.—(*Rindfleisch.*) (PARTLY DIAGRAMMATIC.)
Parts of three lobules are shown. In the center of the lobule, immediately surrounding the vein, hepatic-vein zone, and at the periphery of the lobule, portal-vein zone, are many but slightly altered liver cells. The intermediate area, hepatic-artery zone, is occupied by amyloid material, which has taken no stain and appears as a homogeneous, almost hyaline, body.

Amyloid or **albuminoid infiltration** consists of an infiltration, into the liver, of the so-called amyloid material. The infiltrated agent is deposited in the intermediate or hepatic artery zone of the liver lobule; the causes are those of amyloid infiltration in general. (See p. 111.)

Morbid Anatomy.—The organ is very much increased in size, its margin rounded, its capsule smooth and free from thickening; the tissue is firmer and more elastic than normal,

contains little fat, is pale and bloodless; the cut surface responds to the chemic and stain reactions commonly given by amyloid material.

Morbid Histology.—The infiltrated matter has displaced the liver cells in the affected area.

Pigmentary infiltration of the liver occurs in connection with chronic malaria, and is associated with other lesions which give the organ the name of *malarial liver*. The cause of the process evidently lies in two conditions, (1) the repeated engorgement which occurs as a result of the malarial paroxysm, the liver being enormously distended with blood at each chill, and (2) that blood undergoing the hematolytic changes induced by the malarial parasite, has free coloring-matter liberated from destroyed liver cells. The pigment circulating in the blood is deposited in the liver tissue and gives rise to the peculiar color by which the organ is readily recognized.

In pigmentary infiltrations of the mucous membranes, such as anthracosis, the pigment may reach the liver and be deposited in the connective tissue which surrounds the portal vessel, giving rise to a certain amount of pigmentation of the organ.

Morbid Anatomy.—During life, when distended by blood, and where the process is not combined with cirrhosis, the organ is larger than normal; postmortem it is usually smaller than normal, but the rounded margin indicates that the shrinking has been a postmortem process. The surface is wrinkled, but can be rendered smooth by stretching. The color is a grayish-brown or slate color, due to the deposited pigment; this grayish-lead color has given the organ the name *slate-colored liver*. The organ is more or less flabby or flaccid, and cuts with more resistance than the normal organ, and, on section, oozes considerable blood and pigmented serum; the gall-bladder is small and does not come to the margin of the liver, while the contained bile is likely to be thick and ropy.

Under the microscope there is found, disseminated throughout the organ, around the lobules, and in the perivascular intralobular structures a blackish pigment—altered blood coloring-matter, melanin. Associated with this pigment deposit there is likely to be considerable increase in the connective tissue; this may be so great so as to constitute an actual cirrhosis; the newly-formed connective tissue may be found not only between the lobules but in the lobules.

The degenerations which are most frequent in the liver are parenchymatous degeneration and fatty degeneration.

Parenchymatous degeneration of the liver is found in connection with high temperatures, septic infectious processes, etc.; the organ is swollen, usually pale, and the cut surface cloudy and opaque, not shining and translucent like the normal; the bile elaborated by such an organ is deficient, and may be physiologically inert.

Morbid Histology.—The liver cells are granular, and show the initial changes observed in beginning fatty degeneration. By some it is believed that the change is one of beginning catarrhal inflammation of the lobule, analogous to those observed on the mucous surfaces in the stage of catarrhal inflammation when desquamation is impending. (See p. 121.)

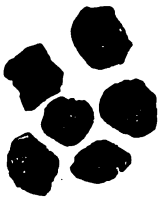

FIG. 259.—GRANULAR DEGENERATION (CLOUDY SWELLING) OF THE LIVER CELLS.—(*Schmaus.*)

Fatty degeneration of the liver, also known as *acute yellow atrophy of the liver*, *malignant jaundice*, and *icterus gravis*. The cause of this condition is not known, but the feeble tendency to epidemicity, the fact that the etiologic agent attacks individuals in groups,—*e. g.*, many cases occur in a single locality among the pregnant women,—taken with the character of the symptoms and lesions, indicates a possible infectious agent. The disease is most common in women,

and is usually seen between the ages of twenty and thirty. As before stated, the changes induced by phosphorus and arsenic are analogous, but not identical.

Morbid Anatomy.—The organ is much reduced in size and weight, is flabby, and, in advanced cases, may be folded over upon itself; as a whole, the consistency may be almost that of a bag of fluid—semifluctuating; the capsule is wrinkled. The color is a dirty yellow and not uniform; in some cases hemorrhages, just under the capsule, may be seen. While the organ may cut with considerable firmness, the semifluid condition of its contents is shown by the fact that large quantities of hepatic tissue may be extruded through a small incision. The cut surface is mottled yellow or yellowish-red in color; there may be hemorrhage into the organ, although this is more common in other viscera than in the diseased liver.

Morbid Histology.—The liver cells are indistinct in outline and advancedly fatty; all stages of fatty degeneration are recognizable; cloudy and granular cells, and cells containing minute oil globules. Occasionally, areas occur in which the cells are no longer recognizable. The fat seen in the liver cell is both in and around the nucleus, and exists as minute drops or oil globules, in contradistinction to the large drops found in fatty infiltration. All zones of the liver lobule are invaded in rapid succession, apparently the outer or portal-vein zone first. In some cases the connective tissue between the lobules is normal; in others it shows a tendency toward proliferation. Some observers are inclined to regard the process as inflammatory; others, as a purely degenerative change depending upon the destruction of hepatic tissue by a poison the exact nature of which is unknown.

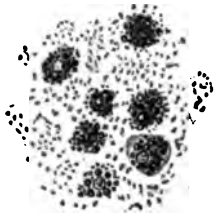

FIG. 260.—FATTY DEGENERATION OF THE LIVER CELLS.—(*Schmaus.*)

The changes observed in the other organs are hemorrhages, especially from the mucous and cutaneous surfaces; the kidneys are granular, the spleen congested, and there may be fatty degeneration of the heart.

Coagulation necrosis, as seen in the liver, occurs in typhoid fever, diphtheria, and allied infectious processes; the organ usually shows cloudy swelling; the areas of coagulation necrosis are minute pin-point spots, whitish or yellowish-white in color, and under the microscope these areas appear as hyaline, degenerated, or dead masses of liver tissue, with fragmentation of the cell nuclei.

Inflammations which occur in the liver are: (1) Suppurative; (2) chronic interstitial; and (3) chronic infectious.

(1) *Hepatic suppuration* occurs in three forms: (1) Traumatic abscess; (2) embolic or pyemic abscess; and (3) the so-called tropic abscess.

(1) **Traumatic Abscess.**—Where injury has been received over the liver and transmitted to that organ, it is probable that, in the process of repair, opportunities are afforded for the localization of any pyogenic bacteria which may be circulating in the blood, and an abscess is thereby engendered; injury due to bruising, foreign bodies finding access to the liver, such as pins, needles, fish-bones, etc., also act as causes by producing infection or giving rise to an area of reduced resistance favorable for the localization of pyogenic organisms. Cysts of the liver may suppurate after the most trifling injury.

A traumatic abscess is usually solitary, and presents no lesion distinct from that of abscess elsewhere. It is, of course, associated with bacteria of suppuration.

(2) **Pyemic abscess** is usually multiple, and where there is a large solitary abscess in pyemia it is probably due to the coalescence of many small foci. Infected emboli may reach the liver through the hepatic artery, or from infected thrombi in the portal vein.

(3) **Tropic abscess** is usually solitary, although there may be two or more; it is usually in the right lobe; the wall has no distinct surrounding membrane: (*a*) The inner layer of the wall consists of necrotic liver tissue; (*b*) an adjoining layer of functionally inactive tissue, in varying stages of necrosis, surrounded by (*c*) a zone of intense hyperemia; unlike the acute and pyemic abscesses, the pus of the amebic abscess may be sterile, and contain the Amœba coli, to which the abscess is now generally considered to be due. The disease is usually

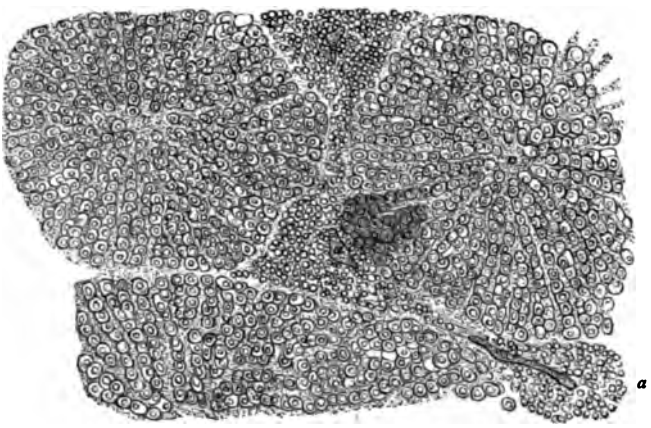

FIG. 261.—BEGINNING CIRRHOSIS OF THE LIVER.—(*Rindfleisch.*) × 300 diameters. *a*, *a*. Interlobular vessels, surrounded by young cell infiltrate. *v*. Hepatic vein.

associated with dysentery due to the amebæ, although occasionally the abscess is found without any distinctly antecedent dysenteric attack.

Cirrhosis of the liver is a chronic interstitial inflammation involving the interlobular connective tissue of the liver.

(1) **Atrophic cirrhosis,** also known as *fibroid liver, granular liver, gin-drinker's liver, hobnail liver, chronic interstitial hepatitis, and contracting, or contracted, liver.*

Causes.—Alcohol, syphilis, red atrophy, malaria, chronic

infections, scarlet fever, rickets, pigmentary infiltration. Many explanations have been offered for the excessive development of fibrous tissue in and around the lobules in cirrhosis. It has been held to be a reactionary inflammation resulting from an

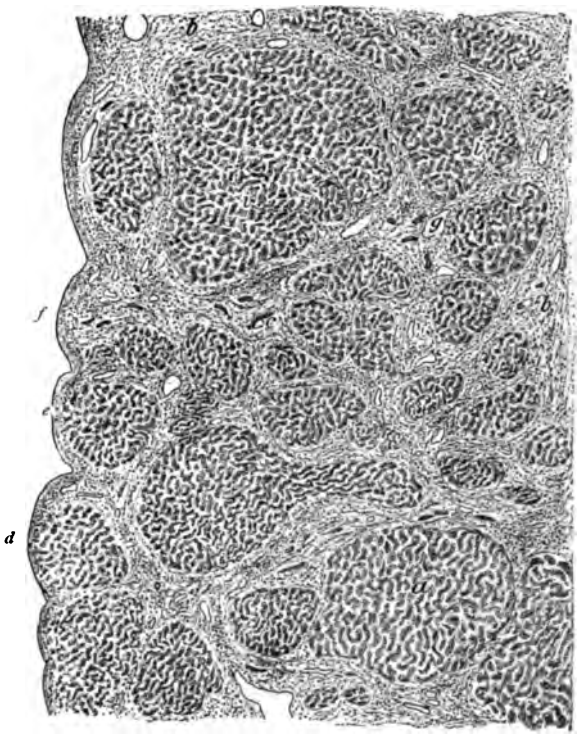

FIG. 262.—ATROPHIC CIRRHOSIS OF THE LIVER, ADVANCED.—(*Schmaus.*) × 50 diameters.

a. Liver lobule. *b*, *b*. Newly-formed fibrous tissue. *c*. Bile ducts. *d*, *e*, *f*. Granules or hobnails on the surface of the liver, due to pulling downward of the newly-formed connective tissue. If the masses are small, they appear on the surface of the organ as granules; if large, they form hobnails. *g*. Branch of portal vein.

irritant brought to the liver by the portal vein, and this, in the light of alcoholic cirrhosis, seems not without reason. By some authorities it is maintained that the initial change is degenerative, the periphery of the lobule being destroyed by

some poison, and that the destroyed or injured zone is replaced by embryonic connective tissue, which goes on to complete organization, and later develops contraction. Weigert inclines toward the last-given explanation.

Morbid Anatomy.—In atrophic cirrhosis of the liver, the organ is diminished in size, not infrequently weighing less than one kilo; the surface is uneven, rough, granular, or hobnailed; the tissue is unusually firm, and cuts with considerable resistance; on section, it presents a yellow, green, or greenish-yellow color; the gall-bladder is usually slightly diminished in size, and the contained bile is watery and dark, although it may be thick and ropy; the bile is less active than normal, and the atrophy of the gall-bladder would indicate that the quantity is diminished.

Morbid Histology.—There is an enormous increase in the fibrous tissue of the liver, and every lobule may be found surrounded by masses of new connective tissue in various stages of development. Contraction of the newly-developed fibrous tissue leads to atrophy of the liver cells, diminution in size, and as the ramifications of the portal vein are embraced in the contracting tissue, there is obstruction of the portal circulation. This obstruction of the portal vein leads to slowing of the circulation in the intestinal and mesenteric branches, to congestion of the intestinal and gastric mucosæ, and a transudate of serum into the abdominal cavity; so great may be the latter that the abdominal cavity may contain from two to four gallons of fluid, and repeated tappings may be necessary to remove the serum which results from the venous stasis. Occasionally, bile ducts may be obstructed by the contracting tissue, and jaundice may ensue, although this is not a common phenomenon. There is some increase of the fat, possibly due to the slowing of the circulation.

In some cases, after long-continued evidence of portal obstruction, as shown by the rapidly-developing ascites, the

blood may find a short circuit from the portal vein to some of the systemic veins, and thereby avoid passing through the contracting fibrous tissue. This short circuiting, by venous anastomosis, occurs through the very much enlarged (1) gastric and esophageal veins; (2) the veins of the round ligament; (3) veins in the suspensory ligament; (4) the inferior hemorrhoidal veins; (5) the veins of Retzius; (6) a single, or, rarely more than one vein, just under the capsule, may make a direct traceable connection between the very much enlarged portal vein and the hepatic vein.

(2) **Fatty Cirrhosis.**—In addition to the increase in the connective tissue, observed in the atrophic cirrhosis, there is in fatty cirrhosis a fatty infiltration, giving rise to an organ which but little resembles the preceding.

Morbid Anatomy and Histology.—The fatty cirrhotic liver is large, usually smooth, but may be slightly granular; the surface may be undulating, is distinctly yellow in color, and presents the rounded edge, etc., already noted as present in fatty infiltration; on section, however, it is very much firmer, contains an excess of fibrous tissue as well as of fat; the fibrous tissue is distributed in the same manner as in atrophic cirrhosis and with the same result, except that the extensive infiltration of fat has enlarged the organ.

(3) **Hypertrophic cirrhosis** is more properly known as *biliary cirrhosis*, and differs from the preceding in that the liver is permanently enlarged and shows no tendency toward contraction; the proliferated connective-tissue cells do not develop into fibrous tissue, but, to a varying extent, retain their embryonal state.

Morbid Anatomy.—The organ is large, much darker than the preceding varieties, and of a greenish-yellow color; the surface is smooth, the margin rounded, the gall-bladder retracted, the tissue firm, and cutting with marked resistance. The cut surface is usually pigmented, bile-stained, and the

newly-formed connective tissue recognizable between the lobules.

Morbid Histology.—There is an abundance of round-cells between the lobules and even extending into the tissue of the lobule. There seems to be an increase in bile ducts, which sometimes form adenoma-like aggregations. By reason of the absence of contraction there is little obstruction of the portal circulation, and hence there is no dropsy. The increased interlobular proliferation may obstruct bile ducts, and commonly gives rise to jaundice.

(4) **Glissonian Cirrhosis,** *Hepatic Capsulitis, or Perihepatitis.*—In this form of cirrhosis the liver is diminished in size, the capsule everywhere greatly thickened, firmly fibroid, sometimes almost cartilaginous in consistency ; the thickened capsule can be readily stripped off, leaving almost normal hepatic tissue beneath, although there is some increase in the interstitial connective tissue.

Syphilis of the liver usually manifests itself as a form of cirrhosis, of which there are two kinds : (1) A diffuse cirrhosis resembling the ordinary form of atrophic cirrhosis. (2) More commonly there are seen—*e. g.*, in congenital syphilis—bands of fibrous tissue, either contracted or undergoing contraction, radiating from the center of the organ to the periphery, and giving rise to contraction in areas, producing the so-called lobulated liver. Such an organ is usually smaller than the normal liver, and is divided by deep, irregular fissures into lobe-like areas varying in number and size.

Gummata of the Liver.—Another form of syphilis of the liver is manifested by the development of gummata. These vary in size, and may be soft, containing, in untreated cases, the products of cheesy necrosis and hyaline change ; when the disease has been treated, the gummata may be converted into fibrous masses with concomitant contraction.

Tuberculosis of the liver rarely occurs as a tubercular

abscess, but more commonly as a miliary tuberculosis distributed throughout the organ.

Leprosy nodules have been observed in the liver, and present the same characteristics as when seen elsewhere. *Actino-*

FIG. 263.—SYPHILITIC CIRRHOSIS OF THE LIVER.—(*Schmaus.*) × 40 diameters.

a. Liver capsule. *b*, *b*, *b*. Newly-formed connective tissue which is grouped in band-like areas, as at *g*. *c*. Branch of portal vein. *l*, *l*, *l*. Liver lobules. *e*. Deep fissure produced in the liver surface by the traction exerted by the fibrous bundles, *g*.

mycosis and *glanders* occur in the liver; they are, however, rare.

Tumors of the Liver.—Adenomata of the liver occasionally occur, and probably arise from the bile ducts with which they are closely associated. These tumors are extremely liable to be cystic; the cyst wall may be papilliferous; occasionally these cystic adenomata are largely composed of dilated bile ducts.

Coccidial disease of the liver is constantly associated with the production of such cysts. *Cancer* of the liver is usually secondary to similar growths in other abdominal viscera—*e. g.*, stomach, pancreas, intestine, genito-urinary organs. *Primary cancer* of the liver is, most commonly, a cylindric-cell epithelioma; *secondary cancer* partakes of the characteristics of the primary growth from which it disseminated. Of the adult connective-tissue tumors, *fibromata*, *angiomata*, and *lymphangiomata* occur; other members of the group are rare. *Sarcomata* occur as primary and secondary growths; the primary growths are exceedingly liable to be pigmented—melanotic.

Cysts of the liver, in addition to those mentioned above, arise either in the connective-tissue spaces between the lobules or in the lobule or bile ducts; the so-called *cystoma* of the liver is usually a congenital cyst containing colloid or clear fluid surrounded by a wall analogous to a serous membrane. *Hydatids* of the liver occur as single or multiple cysts with a structure peculiar to echinococcal disease. (See "Parasitic Cysts," p. 215; also forms of cysts produced by the echinococcus, p. 350.) Occasionally, small cystic dilatations of the bile ducts result from occlusion of the smaller passages. Rarely, small cysts are found in the liver, their contents a clear fluid, the wall lined by ciliated columnar epithelium.

BILIARY PASSAGES.

Malformations.—Occasionally, the common duct, the duct of the gall-bladder, or the gall-bladder itself, may be absent; in certain cases of jaundice in the new-born the ducts are either absent or non-patulous.

Cholangitis.—The *inflammations* to which the bile passages are liable are restricted to catarrhal inflammations, which extend from the duodenum, and to suppurative inflammations of the ducts; the latter is usually due to gall-stone, although this

is not always the cause. The suppurative inflammations of the gall ducts may arise from, or terminate in, pyemia or septicemia.

Gall-stones, or **biliary calculi,** occur in the gall-bladder most commonly, occasionally in the common duct, and rarely in the liver duct. Structurally, each stone is composed of a nucleus of bile pigment or inspissated mucus, around which is deposited cholesterin either in its amorphous or crystalline form. They may be single or multiple, occasionally the gall-bladder containing hundreds of them. They may give rise to obstruction of any of the ducts in which they become lodged, and this may be followed by catarrhal or suppurative inflammation; reaching the bowel, they may lead to obstruction of that viscus. Ulceration, or even perforation, into the abdominal cavity, some hollow viscus—*e. g.*, stomach or colon —or external discharge of the stone, occasionally occurs.

QUESTIONS.

(1) Give malformations and malpositions of the liver. (2) To what diseases is the liver liable? (3) What is red atrophy of the liver? give causes, morbid anatomy, and morbid histology. (4) Under what conditions may hypertrophy of the liver occur? (5) What are the forms of atrophy of the liver? (6) What infiltrations occur in the liver? (7) Give morbid anatomy and morbid histology of fatty infiltration of the liver. (8) Give same for amyloid infiltration. (9) Give forms of pigmentary infiltration, and describe the liver pigmented by malarial disease. (10) To what degenerations is the liver liable? (11) Describe a liver showing parenchymatous degeneration. (12) What is acute yellow atrophy of the liver? give synonyms, morbid anatomy, and morbid histology. (13) Under what condition does coagulation necrosis occur in the liver? (14) Give the forms of hepatic inflammation. (15) Describe and give causes of (*a*) traumatic abscess; (*b*) pyemic abscess; (*c*) tropic abscess. (16) What is cirrhosis of the liver? give synonyms and causes. (17) How many forms of cirrhosis are recognized? (18) Give morbid anatomy and morbid histology of atrophic cirrhosis. (19) Give same for fatty cirrhosis. (20) Give same for hypertrophic cirrhosis, also give synonyms. (21) Give synonym and morbid anatomy of Glissonian

cirrhosis. (22) How do you account for the ascites which accompanies atrophic cirrhosis? (23) How does nature attempt to overcome or avoid obstruction? (24) How may syphilis affect the liver? (25) What other chronic infections occur in the liver? (26) What tumors occur in the liver? (27) What cysts occur in the liver? (28) What morbid conditions occur in the biliary passages? (29) What malformations occur in the biliary passages? (30) What inflammations occur in the biliary passages? (31) Give structure, location, and results which may follow biliary calculi.

CHAPTER X.

PANCREAS.

Normal Structure.—Histologically, this organ is a reproduction of the salivary glands, consisting of acini, with smaller ducts emptying into a larger duct (Wirsung's duct), the latter terminating in the duodenum in common with the hepatic duct.

Malformations and **malpositions** of the organ are of extraordinary rareness. An *accessory pancreas* has been noted. It is usually small and attached to the stomach or intestine.

Hyperemia occurs in the initial stage of inflammation and as a physiologic process during digestion.

Congestion accompanies venous stasis in the abdominal cavity, tumors, cirrhosis of the liver, etc.

Hemorrhage into the pancreas (**pancreatic apoplexy**) is now a recognized morbid process, and occurs as a hemorrhage into the gland structure and as an interstitial or peripancreatic hemorrhage. The process is commonly fatal by implication of the solar plexus, or terminates in hemorrhagic inflammation.

Fatty infiltration of the pancreas is uncommon, and may be a part of general obesity, or may occur in the aged independent of any large amount of fat elsewhere. *Calcareous infiltration* may accompany the lesion.

Cloudy swelling in the pancreas may be associated with similar lesions in the liver and kidneys, and arises from similar causes.

Pancreatitis occurs in two forms—acute and chronic. The former is divided into: (1) *Acute hemorrhagic;* (2) *acute suppurative;* (3) *acute gangrenous.*

(1) **Acute hemorrhagic pancreatitis** occurs in alcoholics and individuals suffering from recurrent attacks of indigestion; as a rule, the patients are over thirty years of age.

Morbid Anatomy.—Extravasation of blood, as already described in pancreatic hemorrhage. The hemorrhage is likely to extend or infiltrate surrounding tissues, or be manifested as separated islands of hemorrhage in the mesentery, mesocolon, or omentum. The disease may be accompanied by the *fat necrosis* of Balser, as shown by white, opaque specks in the interlobular structure of the pancreas, associated with degenerative changes in the adjacent gland-cells. The areas of fat necrosis may be disseminated in other abdominal organs and in the fat of the anterior wall. Langerhans is quoted by Osler as having "shown that this substance is a combination of lime with fatty acids." Fat necrosis may occur independently of pancreatitis. (See p. 130.) There is likely to be some increase in the connective tissue of the pancreas.

(2) **Acute suppurative pancreatitis** occurs as multiple abscesses of small size or as a larger solitary abscess. The cause of the infection—that is, the route by which infection occurs—has not been demonstrated. The presence of bacteria from the alimentary canal in certain of these abscesses points to a possible source of the infection. The process may assume a chronic element as to time; rupture of the abscess into the peritoneum is likely to occur.

(3) **Acute gangrenous pancreatitis** may follow the hemorrhagic form or occur independently of hemorrhage; it may involve the entire pancreas, or a part. The area involved undergoes complete necrosis, and may be discharged by the bowel; acute peritonitis, with fatal termination, is more common.

Chronic pancreatitis consists of a sclerosis of the organ, due to increase of fibrous elements in the interlobular connective tissue. The altered stroma of the organ interferes with the nutrition and function of the parenchyma.

Tuberculosis and **syphilis** of the pancreas occur, but are very rare.

Tumors of the Pancreas.—*Cancer of the pancreas* is the

only neoplasm deserving of consideration. It is almost invariably a scirrhus, and occurs as a primary growth, although cancerous growths in surrounding viscera may invade the pancreas by contiguous spread. *Secondary cancer* of the pancreas—cancer by metastasis—is very rare. When cancer occurs in the pancreas, it is the head of the organ which most commonly suffers. Soft cancers have been found in the pancreas, but are rare. Other neoplasms are exceedingly rare, although not unknown.

Cysts of the pancreas may arise from occlusion of the duct of Wirsung by stricture, pressure of tumors or of surrounding inflammatory growths, or from stone. Cysts may be of almost any size, and have been diagnosticated as ovarian. The fluid may be clear, but is most frequently brownish or chocolate-colored. When solitary, the condition is known as *ranula pancreatica;* when multiple, *cystic disease of the pancreas.* When very old, the cyst may resemble an aneurysm, in that its wall may be calcareous, and hemorrhage into the cavity may leave clots in varying stages of organization or disintegration.

Pancreatic calculi usually occur as round or oval, gray or grayish-white concretions, composed of lime salts and attaining the size of a hazelnut; most commonly they are about the size of a grain of sand two to four mm. in diameter.

QUESTIONS.

(1) What malformations and malpositions may occur in the pancreas? (2) To what diseases is the pancreas liable? (3) What is pancreatic apoplexy? (4) What infiltrations may occur in the pancreas? (5) Give forms of pancreatitis. (6) Give pathology of acute hemorrhagic pancreatitis. (7) Give forms of suppurative pancreatitis. (8) Give morbid anatomy of gangrenous pancreatitis. (9) Give pathology of chronic pancreatitis. (10) What is the most frequent tumor of the pancreas? (11) What is pancreatic ranula? (12) Describe a pancreatic cyst. (13) What is the gross appearance of pancreatic calculi? (14) What is the fat necrosis of Balser?

CHAPTER XI.

URINARY ORGANS.

KIDNEY.

Normal Structure.—The kidney varies somewhat in size; normally, it weighs between 170 gm. and 210 gm. The pyramid is the anatomic unit; the Malpighian tuft, with its blood-vessels and the tube passing off as the proximal convoluted tube, the loop of Henle, the second, or distal, convoluted tube, and terminating in the conducting tube, constitutes the gland unit.

Histologically, the tubules are mucous membrane tracts in which different portions of the tube are lined by epithelial cells having slightly different characteristics. The epithelium of the tuft is flat, with a tendency to cubic outline; the epithelium of the convoluted tubes is more or less polyhedral. The cortex of the organ is made up of two histologic structures, which are most important from a pathologic standpoint; these are the labyrinth and medullary rays or pyramids of Ferrein. In a perfectly normal kidney, these two elements can not be differentiated with any clearness by the unaided eye; but let inflammation occur, the lesions be marked, and the structures named are outlined with remarkable clearness. The thickness of the cortex varies considerably in health, and also depends on the size and general contour of the organ. Some kidneys are short with a thick cortex, other kidneys are long with a somewhat thinner cortex; there is, however, a more or less definite relation between the cortex and the medullary portion, which is sufficiently constant to be utilized for comparison. If a pyramid be selected which is cut through

from apex to base, and a line be stretched from the apex of the pyramid to the capsule, it will be found that two-thirds of the line will be resting upon the medullary portion of the

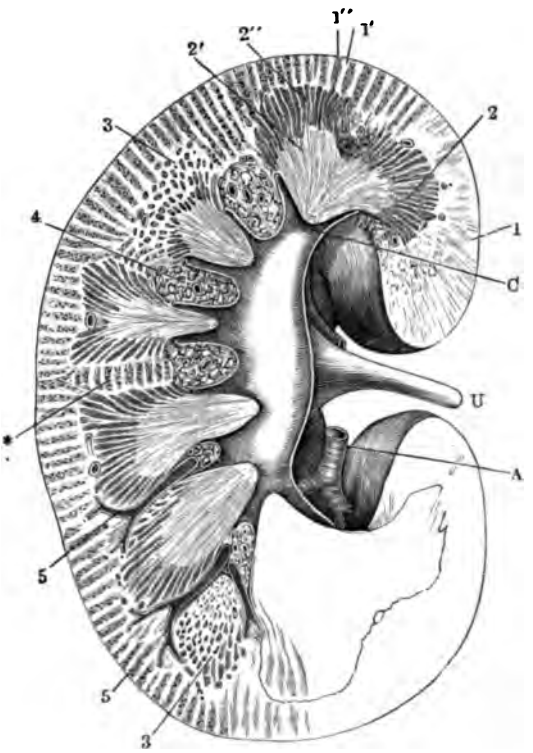

FIG. 264.—LONGITUDINAL SECTION OF THE KIDNEY.—(*Tyson, after Henle.*)

1. Cortex, equal in thickness to about one-half the length of the medullary pyramid. 2. Medulla. C. Pelvis, with calices extending outward between the papillæ of the pyramids. 1'. Medullary rays, between which are the labyrinths 1''. 2'. Conducting tubules of the medulla. The line from 2'' runs to a point just below the cortico-medullary line. A. Renal artery; at 5, 5 is shown its method of distribution. 3, 3. Transverse section of tubules. 4. Fat of renal pelvis. * Transversely coursing medullary rays. U. Ureter.

pyramid and one-third upon the cortex; this rule is not absolute, but the sources of error are so slight that the rule is generally applicable, and, by applying this method of measure-

ment, one can usually tell, at least approximately, whether the cortex is normal in thickness.

Malformations and Malpositions of the Kidney.—It is necessary to consider these conditions together, as malformed kidneys are not, as a rule, in their normal positions.

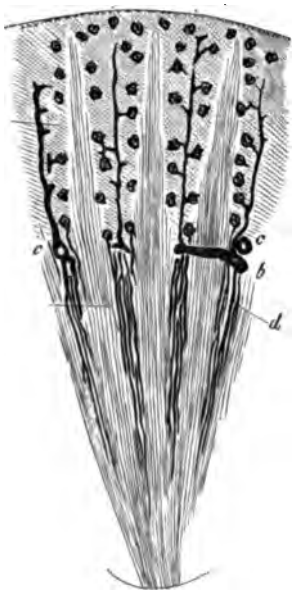

FIG. 265.—DIAGRAM OF BLOOD SUPPLY TO KIDNEY.—(*Rindfleisch.*)

b. Artery at corticomedullary line, the same as 5 in figure 264. *c*, *c*. Blood-vessels passing up to Malpighian tufts in the cortex. *d*. Blood-vessels passing downward into medulla.

The **solitary kidney** represents a blending of the two organs and their development as a single mass. As a rule, the solitary kidney has a duplicated blood supply; it lies in the median line or slightly to one side, and is very much nearer the pelvis than the normally placed organs; indeed, it may be on the brim or even in the pelvis. Commonly, there is but one ureter, although there may be two ureters or a single ureter dividing into two before it reaches the bladder, or two ureters uniting into one just before the bladder is reached. The organ is likely to be floating, although it may be firmly attached.

Horseshoe Kidney.—Next to the solitary kidney, in point of malformation, is the horseshoe kidney. In this condition the two kidneys may be one continuous mass, or they may be considerably separated, with a fibrous band uniting them. The horseshoe kidney lies with its convexity downward, usually has two pelves and two ureters; very rarely, the horseshoe kidney may be to one side of

the median line. The blood-vessels to such kidneys are usually abnormal, in that they arise from or join the larger blood-vessels lower than normally.

A **single kidney** is one more or less normal kidney, having the blood supply of the normal kidney. It is due to arrest of development of the opposite organ, and differs from the solitary kidney in that it does not, histologically or anatomically, although it may physiologically, represent the two organs. It is usually in the normal position, but, having enlarged, its increased weight sometimes leads to loss of anchorage, and, consequently, some form of acquired malposition.

Absence of the Kidney.—Rarely, both kidneys may be absent; absence of one kidney is not so uncommon. Usually it is the left kidney which is absent; the remaining organ hypertrophies and performs the function of two kidneys. The kidneys are not uncommonly lobulated, retaining this characteristic of life.

Floating Kidney.—A kidney otherwise normal may be pushed forward, developing as a floating organ having a pedicle made up of its own blood-vessels, ureter, and fold of the peritoneum, these constituting what is known as the mesonephron.

Movable kidney differs from the preceding in that it is movable behind the peritoneum, and may descend as far as the brim of the pelvis. The condition is most frequent in the female. Movable and floating kidneys are likely to suffer from hydronephrosis, as the result of twisting or kinking of the ureter.

Malformations of the Ureter.—Rarely, the ureter may be imperforate, or, the reverse, sacculated; occasionally, one kidney may have several ureters.

Malformations of the Bladder, Urethra, etc.—Occasionally, the bladder may be bifid; sometimes there is a fissure of the abdominal and vesical walls, giving rise to **ecstrophia,**

fissura, or **inversio, vesicæ**; rarely, the bladder is fissured in its posterior wall, and thereby communicates with the pelvic cavity or with the vagina. The urethra may be **imperforate,** or the bladder and bowel may have a single opening; **rarely,** the bladder may be absent. The urethra may open on the dorsal aspect or on the inferior surface of the penis, giving rise to **epispadias** and to **hypospadias,** respectively. Occasionally, the urethra may have more than one external orifice; in rare instances the urethra opens behind the scrotum, giving rise to **hypospadias perineoscrotalis.**

Diseases of the Kidney.—For pathologic study it may be considered that the portion of the kidney which does the work is the cortex, and that the medullary portion is largely conducting, so that, for a general division of the diseases of the kidney, we may speak of (1) diseases of the secreting structure, meaning thereby disease of the cortex, and (2) disease of the conducting portion, meaning thereby disease of the pyramids and pelvis of the organ. The diseases of the cortex are considered as the so-called *medical diseases* of the kidney; in the diseases of the medullary structure and of the pelvis are embraced the so-called *surgical diseases* of the kidney. This division is purely clinical, but has some foundation, in that the lesions which actually manifest themselves are, to a certain extent at least, in the structures just indicated, as we shall see as we study them.

Hyperemia of the kidney is induced by exposure to cold, by the administration of irritant substances normally excreted through the kidney, and it also occurs in some febrile conditions, but not in all, and in the initial stage of acute nephritis.

Morbid Anatomy.—The organ is somewhat larger than normal, soft, and, on section, drips blood. The cortex is very much darker than that of the normal organ, and is striated, while the medullary portion may be almost purplish. Microscopic examination will show distention of the entire vascular area,

and at points rhexis may have occurred; cloudy swelling is extremely likely to accompany the condition.

Congestion of the kidney arises as the result of impeded venous circulation, such as may occur in chronic heart or lung diseases, or, locally, from pressure on the renal veins by abdominal tumors, ascites, and a very much enlarged pregnant uterus. The most advanced form of congested kidney is the so-called **cyanotic kidney** of chronic heart disease.

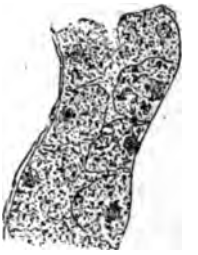

FIG. 266.—CLOUDY SWELLING OF THE EPITHELIUM LINING A KIDNEY TUBULE.—(*Flütterer.*)

Morbid Anatomy.—The organ is large and swollen, and may drip blood on section. The tissue is more firm than normal and resists cutting and tearing, due to the increase in connective tissue; unlike interstitial nephritis, the capsule strips more easily than normal; the cortex is of a deep-red color and striated, the pyramids purplish. Microscopically, the epithelium is cloudy, may be granular, and at points almost fatty; there is some increase in the interstitial connective tissue, as shown by a small round-cell exudate between the tubes, and also an increase in the fibrous tissue—an evidence of past exudation. The blood-vessels are intensely engorged, but there is less likely to be evidence of rhexis than in the condition of hyperemia.

Acute Bright's disease, also known as *acute diffuse nephritis*, *acute nephritis*, *tubular nephritis*, *acute parenchymatous nephritis*, *catarrhal nephritis*, and as *fibrinous nephritis*, arises as the result of overwork or the application of irritants to the kidney, or both causes acting together.

The increased work may be due to cold or exposure, to suppression of cutaneous functions, as in burns, scalds, and extensive skin lesions from other causes. The application of irritants to the kidney arises as a result of the administration

of turpentine, cantharides, chlorate of potash, carbolic acid, and, occasionally, follows the administration of cubebs and copaiba. The acute nephritis which accompanies the infectious fevers, particularly scarlet fever, and the same lesion arising in the course of such diseases as typhoid fever, diphtheria, septicemia and other blood mycoses, probably arises as the result of an attempt on the part of the organism to excrete, through the kidney, some substance which is an irritant to the already overworked organ. The same is true of the acute nephritis which at times accompanies gestation, although it is held, by some authorities, that pressure upon the veins from the kidney, by the enlarged uterus, is partly responsible for the lesion.

The toxic agents which induce this form of kidney inflammation are, no doubt, of many kinds; they may, however, be divided into three groups:

(1) Those arising as products of tissue metabolism, exclusive of the influence of bacteria.

(2) Bacterial poisons.

(3) Toxic agents introduced from without—in other words, poisons, in the ordinary acception of the term.

Morbid Anatomy.—In the earlier stages of some cases of acute nephritis there may be but little alteration in the macroscopic appearances. As a rule, early in the inflammation the organs are intensely swollen, the capsule tense, and, on incision, retracting, thus showing the abnormal tension of the inclosed kidney structure; the surface may drip blood; it is dark and striated, the striæ becoming evident as a result of the intensely engorged condition of the labyrinth, the area composed of convoluted tubules and Malpighian tufts. The capsule strips off with unusual readiness. As the disease progresses, the surface will be more yellow and less hyperemic; striation will still be visible, but will be altered in that the indistinct red lines of the cortex will be displaced by lines of yellow striation, due to the

granular and fatty change beginning in the convoluted tubules and tufts; swelling will be evident, but now it is not so much the enormous increase in blood as it is the swelling of the epithelium in the tubule and tuft.

Histology.—In the earlier stage, first described, there will be found an intense engorgement of the vascular loops within the tufts, which may be enormously distended, and hemorrhage will probably have occurred within the tuft capsule. The epithelium will be found intensely swollen and somewhat granular; the tubules may contain blood-casts. Blood-casts will also be found in the urine. A little later the capillary system will not show such engorgement as that just described; the Malpighian tuft will be hyaline, and the epithelial lining swollen, desquamating, possibly granular, and, in rare instances, fatty; there is likely to be some proliferation of the connective tissue between the tubes and leukocytic infiltration of the connective tissue around the tuft. Further down in the tubules the epithelium will be cloudy, or, it may be, finely granular or hyaline, and may show fatty, associated with granular, change. The nuclei of the epithelial cells are indistinct, granular, or unrecognizable. Between the tubules, in ordinary cases, very little change occurs; there may be some swelling and a few leukocytes scattered through the interstitial tissue of the cortex. In graver or more protracted cases, more or less of the interstitial connective tissue shows the result of proliferation, and a varying amount of round-cell intertubular infiltration may be present.

Changes in the Urine Which Accompany the Changes in the Kidney.—In the earlier stage, with marked hyperemia and hemorrhage into the tufts, there is likely to be an enormous reduction in the amount of urine, which is high colored, smoky, or even darker in hue, and of high specific gravity. The sediment contains an abundance of desquamated epithelium, blood, and casts. In the earlier stages the casts are

made up of blood, which greatly diminishes in amount as the hyperemia is relieved: following the blood-casts, the epithelial cells form the casts, and as these undergo the various changes from cloudiness to advanced fatty degeneration, the condition of the kidney may be inferred by the predominating change observed in the casts. The various forms of casts are figured in the chapter on "Microscopic Examination of Urine." (See pp. 67 and 68.)

The amount of albumin present in the beginning may be so great that a small test-tube containing the urine, if immersed in boiling water, may have its contents fully solidified. As recovery proceeds, the epithelium seen in the casts improves and eventually disappears; a few hyaline casts continue for a short time, but gradually no more can be found; the albumin slowly diminishes and eventually disappears, the reduction in urea is fully made up, and the kidney resumes its normal functions. Where the disease is progressing into the chronic form, epithelial cells, as seen in the casts, do not return to anything like their normal condition, but remain more or less granular and sometimes fatty; the amount of urine remains diminished, urea excretion does not rise to the normal, and albumin persists in a varying quantity.

In acute nephritis cardiovascular changes do not occur; anemia is a marked symptom; edema, anasarca, and effusion into the serous cavities, accompany the more marked cases. Evidences of systemic poisoning, due to the retention of the products of tissue metabolism, may be manifest clinically, although they are rarely, if ever, demonstrable postmortem.

Termination.—This is largely dependent upon the early withdrawal of the cause; if repair began before the production of any new tissue in the interstitial structure, the organ may be completely restored; if a large quantity of new connective tissue has formed, there must be more or less permanent injury; greatly impaired organs, or cases in which the

cause is long applied, may terminate in chronic parenchymatous change.

Chronic parenchymatous nephritis, also known as *chronic diffuse nephritis, chronic desquamative nephritis, chronic tubal nephritis, large white kidney*, etc. This condition may arise (1) as a sequence of the acute inflammation already described; (2) occasionally it comes on insidiously, without any distinctly antecedent inflammatory disorder. In the latter group of cases are included those which are believed to follow overwork of the kidney, as in beer drinkers and consumers of large quantities of alcohol; chronic suppuration and chronic infections, such as tuberculosis and syphilis, are assumed to be, at times, etiologic factors; the disease occasionally follows acute febrile processes, and has been observed after prolonged malarial infection; it may accompany, or follow, or be followed by, amyloid disease of the kidney. Chronic parenchymatous nephritis is a disease of young adults and, occasionally, of children.

Morbid Anatomy.—Two forms of chronic parenchymatous nephritis are recognized, one in which the organ is large, and one in which the organ is small. The former is known as the *large white kidney* or *large fatty kidney*, and the latter as the *small white kidney* or the *pale granular kidney.*

In the large white kidney the organ is very much enlarged, pale, white, or yellowish-white, the capsule thin and may appear edematous; scattered at irregular intervals over the surface will be seen stellate veins, usually intensely distended. On section, the swelling is manifested by the retraction of the capsule as soon as it is incised; the cortex is enormously swollen, and may be as thick as the medulla. It bulges forward and stands out prominent; the pyramid appears slightly sunken; the cut surface is pale, yellowish-white, and at points may be opaque; in contrast to the yellowish-white color of the cortex, the pyramids are dark.

Histology.—The epithelium of the tubules is granular, fatty and desquamating; many of the convoluted tubes will b

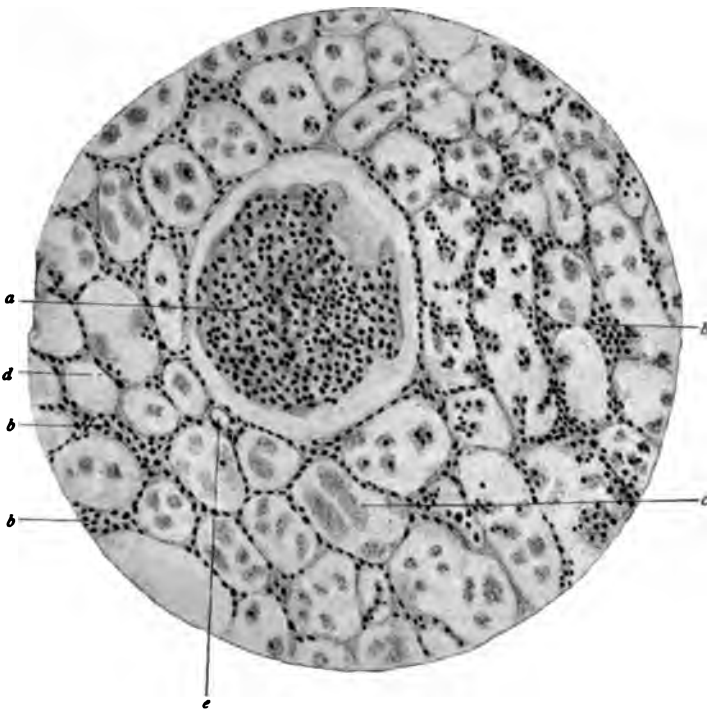

FIG. 267.—CATARRHAL NEPHRITIS. (⅛-inch objective, 1-inch ocular, slightly reduced. Tissue hardened in corrosive sublimate, infiltrated with paraffin, and stained with hem toxylin and eosin. *a*. Malpighian tuft, containing an unusual number of nuclei. *b*, *b*, Points at which there is some slight increase in the interstitial tissue. This is not, ho ever, at any point marked. *c*. Tubule containing granular, degenerating, epithelial cel which have coalesced. In the many tubules shown, the fragmented and desquamat epithelial cells in all stages of granular change are to be seen. In no tubule are t epithelial cells normal or normally arranged. *d*. Tubule from which the epitheliu has all desquamated and been discharged. *e*. Blood-vessel. (Kidney from a case tubular nephritis which terminated in death from eclampsia at the end of elev weeks after the appearance of the first symptoms.)

found distended with hyaline, fatty, or granular casts. Th epithelium of the tufts is desquamating, and shows the sam changes already described in the tubules. The capillaries

the tufts are likely to be hyaline; the capsule of the tufts and the basement membrane of the tubules are both likely to be slightly increased in thickness, and the intertubular connective tissue may be increased, but this increase is usually slight; there is, however, marked swelling.

In the *large white kidney* there is a tendency toward the development of hemorrhage in the cortex, and these areas may be found postmortem as brownish or yellowish-brown spots. The hemorrhage is probably due to increased vascular tension without corresponding increase in the thickness of the capillary walls; or the fatty changes in the perivascular tissue may so weaken that structure as to withdraw the normal support to the blood-vessel, thereby favoring rhexis.

The *small white kidney* differs from the preceding in that its surface is granular, its capsule more adherent, its cortex less swollen; indeed, the latter may be thinner than that of the normal organ; the kidney is firm, and cuts with more resistance than the normal. Histologically, the same tubular and tuft changes, as already described in the large white kidney, will be found present; there is, however, a marked increase in the connective tissue, more marked in some places than in others; many of the tufts will be found atrophied, and many of the tubules compressed or occluded by the contraction of the newly-developed connective tissue.

If one looks merely at the pathologic picture which this type represents, he is led to view the condition as one of chronic tubular inflammation, with superadded interstitial change. As we will see later, there are many of the elements present to be noted in the chronic interstitial nephritis, and, as already described, many of the elements noted in the parenchymatous nephritis, and there is no pathologic reason, either etiologic or anatomic, for believing that it is impossible for the two forms of nephritis to intermingle. We can not, at present, absolutely settle this question, so that writers variously classify

and consider the small white kidney, some holding that it is produced in a way entirely distinct from the chronic parenchymatous or the chronic interstitial, others holding that it is but a form of the chronic parenchymatous or a tubular lesion engrafted on an interstitial nephritis, or a parenchymatous nephritis which has persisted sufficiently long to have developed fibroid changes in the intertubular connective tissue. When we consider the kidney as a mucous membrane, we are enabled to see the resemblance between the changes seen in the submucosa after protracted inflammations of the mucous membranes and the interstitial changes observed in the kidney subsequent to a prolonged inflammatory lesion of the tubules.

Changes in the Urine Which Accompany Chronic Parenchymatous Nephritis.—The urine is diminished in quantity, of high specific gravity, usually high colored, albuminous to a marked degree, and commonly contains an abundant sediment, in which will be found all forms of casts which may arise from any structural lesion of the epithelium lining the tubules. Granular and fatty casts, indicating the changes in the epithelium, hyaline and epithelial casts containing leukocytes, and, occasionally, red blood-corpuscles, although these are rare, indicate the inflammatory lesion which is accompanying the process of degeneration. There is a reduction in the excretion of the products of metabolism.

Where the process is long continued and it is probable that the large white kidney is being converted into the small white kidney, or the latter is arising independently, the urine will be more abundant than from the large white kidney, and the albumin will be less. Commonly, the small white kidney seems to more fully perform its functions than the large white organ.

The disease may be accompanied by alterations in the vascular system resembling those of chronic interstitial nephritis; although rare, retinal lesions are not unknown; where the

kidney shows a tendency toward contraction (small white kidney), the vascular and retinal changes are more likely to be present. Anemia and edema are likely to accompany all forms of parenchymatous nephritis, and accumulation of serum in the serous cavities is likely to occur.

Chronic interstitial nephritis, also known as *contracting* or *contracted kidney, granular kidney, fibroid kidney, cirrhotic kidney, gouty kidney, renal sclerosis,* and, occasionally, as *hob-nail kidney,* is a chronic interstitial inflammation of the kidney analogous to interstitial inflammation of other granular viscera—*e. g.*, interstitial inflammation of the liver and interstitial inflammation of the pancreas.

Etiology.—Whether the large white kidney, already considered, ever becomes the kidney which we are at present studying, seems very doubtful; that the small white kidney might eventually terminate in a fibroid organ is possible; but in a large majority of cases, if not in all, this disease is primary and not preceded by any of the lesions which we have already considered. There may be no apparent cause; heredity is a possible influence; continual call upon the kidney for the excretion of irritant materials is probably a most constant factor; examples of this are to be noted in alcoholics, sufferers from gout and lithemia, chronic lead poisoning, and in individuals who subsist upon a diet composed largely of substances whose metabolism terminates in uric acid. Persistent overwork of the kidney may be a factor. As to age, the phenomena of the disease usually manifest themselves only in advanced life—forty years or later; the disease is rare in younger individuals; it is probable, however, that the lesions begin much earlier than the clinical data would seem to indicate.

Morbid Anatomy.—The kidneys are diminished in size and may weigh no more than 100 gm. to 125 gm.; both organs may not be equally involved. The surface of the kidney is uneven, irregular, indurated, and the capsule can not be

cleaned of the perinephritic fat so easily as the normal kidney. The organ is very firm, hard, slightly elastic, and resists cutting to such a degree that it may creak under the knife; the color varies,—it is usually red or reddish, or, where the organ is markedly anemic, may be somewhat pale; it never has the yellowish fatty appearance described in the chronic parenchymatous inflammation. The capsule strips off with great difficulty, and it is firmly adherent to the underlying tissue, part of which may pull off with the capsule. The capsule is markedly thickened, and immediately under it may be found small cysts varying in size from a pinhead to the end of one's thumb, rarely larger; these cysts are near the surface and may be ruptured in removing the capsule. The cyst contents are usually clear or slightly straw colored. In very rare cases there may be hemorrhage into or around the cyst.

In comparing the cortex with the medullary portion, the observer will be immediately struck with the contrast between the condition now being described and the cortex in chronic parenchymatous nephritis. The cortex is irregularly thin, and there may be pyramids in which, macroscopically, the cortex can not be demonstrated. Occasionally, there will be a pyramid which has its normal quota of cortex, thus illustrating the patchy character of the lesion; as a rule, however, the cortex, to the various pyramids, is more or less contracted. The pyramids are but slightly wasted. There is usually considerable fat in the pelvis, which is less capacious than normal.

Morbid Histology.—Sections show that the lesion is patchy and not universally distributed throughout the cortex; here and there will be seen small areas in which the changes are most marked; at other points there will be areas in which very little change will be discernible. The fibrous tissue will be most markedly increased in the labyrinth, less so in the pyramid of Ferrein, and very much less in the medullary portion.

Between the tubules, in the interstitial connective tissue of the organ, will be found new cell-growth in various stages of development; the more recent cellular exudate will be of round-cells. Where organization is in process, these round-cells will

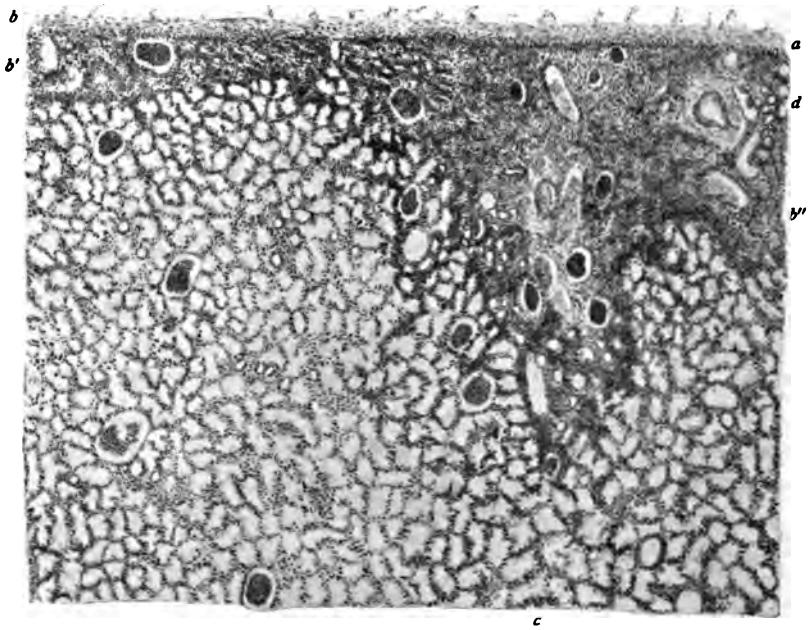

FIG. 268.—KIDNEY, CHRONIC INTERSTITIAL NEPHRITIS. (¼-inch objective, 1-inch ocular, slightly reduced.)

Specimen fixed in corrosive sublimate, infiltrated with paraffin, and stained with hematoxylin and eosin. *a*. Slightly thickened capsule. *b*, *b'*, *b''* and *a* bound the area of most marked interstitial change, although an increase of the interstitial tissue is evident between *b''* and *c*. About one centimeter to the left of *d* is seen a beginning cyst. In the area of most marked interstitial change are a number of degenerating Malpighian tufts, while but a few of the tubules are recognizable. The new tissue is not yet fully developed, but at points, as around the cyst *d*, shows partial conversion into fibrous tissue.

be seen gradually forming into spindle-shaped elements, fibrous tissue eventually terminating the complete organization of the round-cells. The newly-formed fibrous tissue contracts, squeezes upon the blood-vessels, Malpighian tufts and tubules,

thereby lessening the blood supply, the nutrition, and the functional activity of these structures. The glomeruli have their capsules thickened by the new cell infiltrate, which, contracting, leads to destruction of the capillary tuft, preceded or followed by hyaline change. Glomeruli, whose vascular supply is still normal, have thickened capsules; the thickening of the capsule is continuous with the thickened basement membrane of the tubule. The epithelium of the tubules shows various changes dependent upon the influence of the interstitial deposit within any given area. The large, swollen, granular, fatty, tortuous tubules of parenchymatous nephritis are not found; instead, the tubules are diminished in size; in the areas where the new tissue is most rapidly organizing, the gradual contraction may occlude tubules and give rise to distention above the point of obstruction, thereby accounting for the cysts already described. Where the tubule is being influenced by the contraction, the epithelium is atrophied, finely granular, and the cells greatly diminished in size; where the fluids are retained within the tubule, by obstruction below, the epithelium will be flattened, hyaline, granular, or even fatty; occasionally, tube casts may be seen *in situ;* if the epithelium or interstitial tissue be pigmented, it is probably the result of past hemorrhage. The blood-vessels of the kidney show the same changes to be described in the vascular apparatus elsewhere.

The urine is increased in quantity, light in color, and may be almost clear; its specific gravity is rarely over 1012 or 1015 and may fall as low as 1005; albumin is present in varying amounts; sometimes the albumin may be scanty and escape detection, or, for short periods, rarely long, it may be entirely absent; as a rule, there is no sediment and the dissolved solid constituents—salts and urea—are diminished. The casts present are usually hyaline; these are not abundant and not constantly present; during acute exacerbations in the inflam-

matory processes, the phenomena of nephritic hyperemia may be noted.

Changes in the Vascular System.—The heart shows marked hypertrophy, or dilatation, and there is a general arterio-capillary fibrosis or arterial sclerosis. (See p. 429.)

There is likely to be inflammation of some of the serous membranes; hemorrhage in the retina is not uncommon; edema, anasarca, and accumulations of fluid in the serous cavities, such as occur in chronic parenchymatous nephritis, are not likely to be found.

Amyloid disease of the kidney arises in connection with general amyloid disease. (See p. 111.) The process is frequently associated with a more or less fully-developed chronic parenchymatous nephritis, as already described.

Morbid Anatomy.—In the vast majority of cases the kidney is much increased in size; in a very few instances it may not be larger than the normal. The veins of the capsule are dilated, the surface is smooth, the organ firm, but not fibroid. The tissue cuts with more resistance than in chronic parenchymatous nephritis pure and simple; the cortex is much thickened, is glistening or hyaline, slightly swollen, and the Malpighian tufts, in which the lesion is most manifest, may be readily picked out. The pure hyaline or semitranslucent cortex contrasts with the deep red, or almost purplish, medullary portion; the usual test for amyloid disease will demonstrate the character of the process.

The urine is usually abundant, pale, clear, and of a low specific gravity; hyaline, granular, or fatty casts are usually present, and, occasionally,—not constantly, as commonly believed,—waxy casts which may give the amyloid reaction. The changes in other organs and tissues are dependent upon the general amyloid infiltration or upon the character of the accompanying renal change—*e. g.*, if there be parenchymatous nephritis, dropsy, edema, etc., may be present; if attended by

interstitial nephritis, which is rare, the vascular and other phenomena of that condition may be manifest.

Pyelitis and **pyelonephritis,** inflammation of the pelvis of the kidney, and of the pelvis and kidney, the inflammation of the kidney being secondary to that of the pelvis. These inflammations may be catarrhal, pseudomembranous, gangrenous, suppurative, or hemorrhagic; they usually occur in connection with infectious diseases, or may be due to the irritation of drugs excreted by the kidney, such as cantharides, turpentine, etc. In pyemic processes the inflammations are likely to be suppurative, or suppurative processes may invade the pelvis by extension from the bladder.

Stone in the kidney, or stone in the ureter, is constantly attended by some of the forms of mucous membrane inflammation. The same is true of stone in the bladder. Inflammations in these structures may be attended by ulceration, by gangrenous processes, and marked thickening of the submucosa. As a result of prolonged ureteritis, thickening, and induration, the ureter may be constricted,—strictured,—the obstruction thereby produced leading, in time, to hydronephrosis. Occasionally, the infection may extend through the mucosa and invade the perinephritic tissues, giving rise to a condition known as **perinephritic abscess.** Injuries, such as falls and bruises, are said to predispose to abscess formation in the fat around the kidney. Perinephritic abscess may, of course, arise from any pyogenic infection which reaches the fat in which the kidney lies. As already stated, the above forms of inflammation in the conducting apparatus are classed with what are known as the surgical diseases of the kidney.

Cystitis.—*Inflammation of the bladder* may be catarrhal, pseudomembranous, gangrenous, hemorrhagic, or suppurative. Pseudomembranous processes are by far the most rare, the catarrhal the most frequent; suppurative inflammation of the bladder is not uncommon; very rarely the inflammatory

process in the bladder may lead to inflammatory conditions of the connective tissue surrounding the bladder—**pericystitis.** Occasionally, abscess formation occurs in the bladder wall; such purulent accumulations are usually small and multiple, and may rupture into the bladder or externally.

Beside the suppurative and gonorrheal infections of the bladder, numerous bacteria may gain access to the organ from dirty catheters, etc., and give rise to putrefaction of the contained urine, with absorption of bacterial products and general systemic septic phenomena. These are intensified by obstructive diseases which prevent the bladder from emptying itself, such as strictures, tumors, and diseases of the prostate; obstructive lesions also lead to hypertrophy of the muscular coat of the bladder. The bladder may be dilated as a result of obstruction, or paralysis of its muscular wall; *rupture* of the bladder may follow injury, overdistention, perforation by instrument or disease, ulcer, or necrosis. The bladder may communicate by abnormal routes with the adjacent cavities, or externally; such pathologic passages are known as *urinary fistulæ.*

Tuberculosis of the urinary organs may occur as an acute miliary process in the kidney or in the conducting apparatus; the ureter and bladder may be involved. In the more chronic forms of tuberculosis of the kidney,—the so-called *scrofulous kidney*,—the organ may be converted into a mass of caseous nodules varying in size, the larger usually being the size of one, two, or more pyramids. The ureter is occluded by the process in some of the cases. *Tuberculosis of the bladder* or of the prostate, thereby invading a part of the urethra, occurs.

Syphilis of the urinary organs, aside from the external initial lesion, occurs as gummata of the kidney; these may lead to scars in the kidney or may remain more or less hyaline and caseous.

Leprosy rarely invades the urinary organs, although leprous disease of the kidney has been observed.

Tumors.—*Adenomata* occur in the kidney structure. *Papillomata* have been observed in the pelvis. *Carcinomata* are rare, and occur as encephaloid and rarely as hard cancers. Of the adult connective-tissue tumors, *fibromata* are the most common, although others occur; *sarcomata* of the kidney are not uncommon; they are most frequent in children and young adults. Although cancers and sarcomata occur as secondary growths in the kidney, they are not frequent.

Cysts of the Kidney.—*Retention cyst* of the tubule, as seen in contracted kidney, has been described. In the cortex they are usually small, although they may be as large as the end of one's thumb, rarely larger; they are usually multiple, rarely solitary, and are due to the occlusion of the tubule and its dilatation above. *Hydatid cysts* of the kidney are rare.

Gradually-developing occlusion of the ureter gives rise to **hydronephrosis** if the retained material be water; if the contents of the cyst be pus, the condition is known as **pyonephrosis.** Organs showing either of these conditions vary much in size, are usually large, with atrophy of the renal tissue, due to pressure and the retained material in the pelvis. The condition is not produced by sudden occlusion of the ureter, but is dependent, in most cases, upon gradual narrowing or interrupted obstruction of the ureter, such as may arise from kinking, as in the floating and movable kidneys, or pressure on the ureter by tumors, or obstruction by a calculus, or, as stated on a previous page, chronic ureteritis with contraction may so narrow the lumen of the ureter as to induce retention above the point of obstruction. It will be observed that the causes just given act by slowly inducing an obstruction which fails to permit the escape of secretion as rapidly as formed.

A rare, but extremely interesting, cyst in the kidney is the

so-called **cystic disease of the kidney.** As a rule, but one kidney is involved, except in bilateral congenital cystic disease, when both organs may be implicated; such a condition may be sufficiently marked, at birth, as to interfere with delivery. The cystic kidney is large, made up of numerous cysts, and very often showing no recognizable renal tissue; the fluid within the cyst is usually clear, albuminous, and without any evidence of urine. The cyst wall is usually lined by flattened epithelial cells; under the microscope some renal tissue may be found. The process is presumed to be due to some defect in development; as already stated, in the adult the disease is usually unilateral.

QUESTIONS.

(1) What is the normal relation between the cortex and the medullary portions of the kidney? (2) What diseases alter this, and in what way? (3) Give malformations and malpositions of the kidney. (4) What is the solitary kidney? (5) Give malposition and malformation of the horse-shoe kidney. (6) What is meant by single kidney? (7) What is the difference between the movable and the floating kidney? (8) What malformation may the ureter manifest? (9) Mention the most frequent malformation of the bladder and urethra. (10) What is meant by the following terms: Ecstrophia vesicæ? epispadias? hypospadias? hypospadias perineoscrotalis? (11) How are the diseases of the kidney divided? (12) Mention the morbid conditions to which the kidney is liable. (13) What are the medical and what the surgical diseases of the kidney? (14) Give causes and morbid anatomy of renal hyperemia? (15) What is cyanotic kidney? (16) Describe same and differentiate from hyperemia. (17) Give causes of both. (18) What is acute Bright's disease? give synonyms. (19) What are its causes? (20) Give sources of toxic agents which may induce it. (21) Give its morbid anatomy. (22) Give morbid histology. (23) What changes are found in the urine? (24) How would the urine indicate the subsidence of the disease? (25) How its gradual progression into the chronic form? (26) What general morbid processes accompany acute nephritis? (27) Give terminations. (28) What is chronic parenchymatous nephritis? give synonyms. (29) Give its causes. (30) What forms of chronic parenchymatous nephritis are recognized? (31) Give morbid anatomy and morbid histology of each form. (32) Give changes in the urine. (33)

What general changes occur? (34) What is chronic interstitial nephritis? give synonyms. (35) Give causes. (36) Describe such a kidney. (37) Give its histology, and explain the phenomena which terminate in small fibroid organ. (38) What are the urinary changes? (39) What are the morbid processes accompanying the disease? (40) Describe an amyloid kidney. (41) What urinary phenomena accompany the process? (42) What are pyelitis and pyelonephritis? give forms, causes, and terminations. (43) What is perinephritic suppuration and its causes? (44) What is pyonephrosis? (45) What is hydronephrosis? (46) What are the forms of cystitis? (47) To what infections is the bladder most liable? (48) What is pericystitis? (49) Give causes of dilatation of the bladder. (50) Give causes of rupture of the bladder. (51) What is a urinary fistula? (52) What forms, and where does tuberculosis of the genito-urinary apparatus occur? (53) How may syphilis attack the urinary organs? (54) What tumors and cysts occur in the urinary organs? (55) What is cystic disease of the kidney?

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